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SPLENECTOMY FOR ACQUIRED HEMOLYTIC JAUNDICE IN THE AGED*

Report of a Case

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A PATIENT who develops severe hemolytic anemia at the age of seventy and has no past history of this disease presents complex problems in diagnosis and treatment. The age of onset is late for the diagnosis of congenital hemolytic jaundice and, regardless of the diagnosis, the question arises whether splenectomy is advisable at this age. Furthermore, increased fragility of the erythrocytes may be overlooked when the routine test for fragility is done on blood samples showing marked anemia. These problems were met in a seventy-year-old woman in whom splenectomy was performed with recovery. The literature was reviewed to determine the usefulness of splenectomy in the treatment of acquired hemolytic jaundice in patients with the onset of the disease occurring after the age of fifty.

CASE REPORT

M. E. F., a 70-year-old, married woman, was admitted to the Peter Bent Brigham Hospital for the first time on April 15, 1941. The chief complaint was weakness of 3 to 4 months' duration. The family history revealed no case of anemia, jaundice or endocrine disorders; the mother and only brother had suffered from heart disease. The patient had lived in New England all her life, had never been pregnant and gave no history of exposure to any materials known to be injurious to the blood or blood-forming tissue. Systemic review disclosed that the patient's health had always been good in the past.

Four months prior to admission the patient first experienced malaise, increased weakness, fatigability, palpitation and shortness of breath on exertion. She did not complain of paresthesias and gave no evidence to suggest blood loss, bleeding dyscrasia or liver disease. A month later she consulted a physician on account of these complaints. Not until 2 weeks before admission did the skin assume a yellow tint and her physician discover a low red-cell count. Bed rest and the administration of liver extract by mouth during 2 weeks brought no improvement.

On admission the patient appeared to be severely ill, as evidenced by prostration, tachycardia, pallor and a lemon-yellow skin. The tongue was smooth and pale. There was a palpable lymph node in the left supraclavicular region. The blood pressure was 130/40. The heart was slightly enlarged to the left, and there was present a loud blowing systolic murmur, heard best over the cardiac apex. The liver extended 2 cm. below the right costal margin, and the spleen was barely palpable. Neurologic examination revealed no abnormalities.

Significant laboratory data included negative Wassermann and Hinton blood tests. The urine was normal except for a + test for protein. The red-cell count was 870,000, with 17 per cent reticulocytes. The white-cell count was 17,500, with 75 per cent neutrophils, 19 per cent lymphocytes, 4 per cent monocytes and 2 per cent unindentified cells; 2 normoblasts were found among 100 leukocytes. The hemoglobin was 32 per cent (Sahli). The icteric index was 20, and by the Sanford[1] method of erythrocyte fragility determination, hemolysis began at 0.44 per cent saline solution and was complete at 0.42 per cent, a normal result by the method used.

When correction was made for the anemia,[2] the initial hemolysis was found to occur at 0.58 per cent saline solution, whereas a normal control showed the same amount of hemolysis in a 0.44 per cent solution. There was 75 per cent hemolysis in 0.40 per cent saline in the blood; the same degree of hemolysis occurred at 0.35 per cent saline in the blood of the normal control. In addition, the patient's blood gave a negative hemolysis test with acidified serum[3] and contained no hemolysins of the Donath–Landsteiner type, no autohemolysins and no agglutinins in the presence of cold or heat. Plasma hemoglobin amounted to less than 7 mg. per 100 cc., and was considered normal. At that time (3 weeks after admission) the red-cell count was 1,200,000, with 4.9 gm. of hemoglobin per 100 cc. and 29 per cent reticulocytes. The hematocrit reading was 16.6, the mean corpuscular volume 138.3 cubic microns, the mean corpuscular hemoglobin concentration 30 per cent, and the mean corpuscular hemoglobin 42 micromicrogm. The white-cell count was 13,600 with 54 per cent segmented neutrophils, 13 per cent band forms, 4 per cent eosinophils, 21 per cent small lymphocytes, 4 per cent large lymphocytes, 3 per cent adult monocytes and 1 per cent young monocytes. A smear showed moderate anisocytosis; macrocytes and normocytes were seen. There was much polychromatophilia, with some Howell–Jolly bodies, stippling and a few erythroblasts and normoblasts. No spherocytes were seen. The platelets and white cells were normal. A direct van den Bergh test showed 0.9 mg. of bilirubin per 100 cc. of plasma and an indirect one 3.1 mg.§ Roentgen-ray films of the chest, gastrointestinal tract, skull and long bones failed to disclose disease. Gastric aspiration revealed free hydrochloric acid to the extent of 22 units in the sample withdrawn 20 minutes after histamine injection.

Following the injection of six doses, totaling 8 cc., of liver extract (Lederle, *N. N. R.*) and a transfusion of 500 cc. of whole blood, the red-cell count was only 1,430,000, with no increase in reticulocytes. The hematocrit reading was 19, and the icteric index 30. The patient felt improved and was discharged home on May 13, approximately 1 month after admission.

After spending a week at home the patient became so chronically exhausted that she was readmitted. Physical examination at that time was essentially the same as before. The red-cell count was 1,020,000, the hemoglobin 3.75 gm. per 100 cc., the hematocrit 12, and the icteric index 18. The white-cell count was 33,100, with a normal differential ex-

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§The determinations listed were made by Dr. Henry H. Brewster and Miss Geneva A. Daland, of the Thorndike Memorial Laboratory, Boston City Hospital.

cept for 4 per cent normoblasts and 1 per cent megaloblasts. The fragility of the erythrocytes was again studied. By the method of Sanford, hemolysis began at 0.44 per cent saline solution and was complete at 0.34 per cent, both values being within the limits of normal and equivalent to those of a normal control blood tested at the same time. When, however, enough plasma had been removed from the blood of the patient to make the hematocrit reading normal — that is, 40 — and the fragility was again tested by the Sanford method, it began at 0.50 per cent and was complete at 0.40 per cent, values definitely indicative of greater fragility than normal. In order to check the findings of these naked-eye tests, the photoelectric method of Hunter[4] was used, testing blood with a hematocrit level of 17. When fragility was determined by this method, hemolysis began at 0.60 per cent saline and was complete at 0.36 per cent, whereas in the normal control it began at 0.48 per cent and was complete at 0.34 per cent.

During this stay roentgen-ray therapy — two doses of 25r each directed at the entire trunk on successive days — was administered on the supposition that the etiologic process might be neoplastic in nature, and was followed by a fall in the white-cell count from 25,000 to 11,000 and a decrease in reticulocytes from 18 to 6 per cent. It was therefore discontinued. Twelve days and 29 days later the reticulocytes numbered 6 per cent and 9 per cent, respectively.

On June 8, 3 weeks after admission, the patient experienced an attack of severe pain in the right upper quadrant of the abdomen. A mass in the right upper quadrant, corresponding to the gall bladder, became palpable and remained so for 24 hours, after which it could no longer be felt. The findings were interpreted as indicative of obstruction of the cystic duct. Biopsy of the palpable left supraclavicular lymph node revealed tuberculous lymphadenitis. On the 24th day, a biopsy of the sternal bone marrow was performed and was interpreted as showing hyperplasia of the marrow, chiefly erythroblastic in nature, and probably secondary in origin.

Because of the above findings and the failure of the patient to improve on vigorous transfusion therapy, — she received a total of 7600 cc. of whole blood in 1 month, — she was transferred to the Surgical Service for splenectomy. On June 29, the day of her transfer, the red-cell count was elevated to 2,100,000 by repeated transfusions. The following day splenectomy was performed, the patient withstanding the procedure well. She received two more transfusions on the day of operation. On the first postoperative day the red-cell count was 2,600,000. No further transfusions were given.

At operation the gall bladder was seen to be tense and distended. It did not empty on pressure; no stones could be palpated. It was not removed. The liver did not appear abnormal to inspection or palpation. The weight of the spleen was 362 gm. Following is the report on the pathological examination of the spleen:

> The color of the cut surface is dark red. The malpighian bodies are not prominent. There is no grossly evident increased trabeculation. No areas of infarction are encountered. Microscopical examination discloses that the capsule is not remarkable. The malpighian corpuscles are essentially normal in color and size. They are quite active, with sometimes moderately prominent germinative centers. The reticular cords, however, show definite lymphoid depletion, and there is a certain degree of engorgement of the meshes of the red pulp. One of the most striking features is the presence of large amounts of golden-brown pigment consistent with hemosiderin. This is found extracellularly as well as intracellularly. In the latter instance it is within large monocytes, or often within the lining cells of the sinuses. Scattered through the organ there appear to be a somewhat increased number of polymorphonuclear leukocytes. Another striking feature is the presence of foci of hematopoiesis mostly situated near the malpighian corpuscles, and there is also hematopoiesis going on within the sinuses. The number of eosinophilic myelocytes is quite excessive, and occasional megakaryocytes are encountered. The general architecture is well preserved. The sinuses are frequently prominent. The large arteries show only a minimal degree of sclerotic changes, whereas the small arterioles are rather uninvolved. . . . This picture of marked hematopoiesis with extensive hemosiderin deposits is quite consistent with that of a hemolytic anemia.

After an uneventful postoperative course of 11 days, the patient was transferred to the Medical Service, at which time the red-cell count was 3,500,000. She appeared much stronger and happier than at any previous time during the hospital stay. When she was discharged on the 22nd postoperative day, she was ambulatory and the red-cell count was 4,300,000, with 11.5 gm. of hemoglobin per 100 cc., 2.0 per cent reticulocytes and an icteric index of 14.

The patient was seen again 4 months after splenectomy, at which time she looked well and had regained her strength so that she was able to arise at 5:30 every morning. No pallor or jaundice could be detected. The red-cell count was 4,560,000, with 13.5 gm. of hemoglobin per 100 cc. The white-cell count was 8400, with 36 per cent segmented neutrophils, 1 per cent band forms, 52 per cent lymphocytes, 8 per cent monocytes and 3 per cent eosinophils. There were 0.5 per cent reticulocytes. Platelets were plentiful, and the blood smear appeared normal except for the variations in red-cell size described below. No spherocytes were seen.

Fragility tests done by the photoelectric method of Hunter disclosed that the red cells were still definitely more fragile than those of a normal control. In 0.60 per cent saline solution 5.4 per cent of the erythrocytes were hemolyzed, whereas hemolysis did not begin in the control blood until the hypotonicity of the salt solution had reached 0.51 per cent. Ninety-eight per cent of the cells were hemolyzed at 0.36 per cent saline, whereas but 87.5 per cent hemolysis occurred in the blood of the control at this concentration. Fragility tests performed on the blood of the patient's sister and grandnephew, the only relatives available, failed to reveal aberration from the normal.

A Price–Jones curve showed a range of red-cell diameters considerably wider than normal. Of 500 erythrocytes examined, one had a diameter of 3.1 microns, one of 3.5, one of 3.9, and 22 of 4.2. The peak of the curve occurred at 7.0 microns. There were 11 cells with a diameter of 9.1 microns, and 4 with a diameter of 9.8. Price–Jones curves done on the blood of the patient's sister and grandnephew failed to reveal abnormalities.

On March 16, 1942, over 8 months after splenectomy, the patient reported that she was entirely well and more vigorous than she had been at any time in the previous 10 years.

Discussion

This case yields information on three phases of the diagnosis and treatment of hemolytic jaundice. First, the disparity among results obtained with various types of erythrocyte fragility tests deserves comment. Second, an attempt to classify the patient's anemia as either the congenital or the acquired form helps to evaluate recent studies of certain features of these syndromes. Third, the patient's advanced age at the time of onset and of splenectomy is of interest, since only 1 other case of splenectomy for hemolytic jaundice in a patient over seventy years of age has been found in the literature.[5]

Estimation of Erythrocyte Fragility

The Sanford red-cell fragility test, although widely used and usually adequate for the detection of gross changes, gave an erroneous result in this case in the presence of marked anemia. Although a large percentage of the red cells were abnormally fragile, the anemia was so marked that the quantity of blood used in the test did not contain enough such

cells to produce hemolysis detectable to the eye. When, however, the anemia was corrected by removing sufficient plasma to bring the packed red-cell volume to a normal level, the abnormal fragility of the cells was immediately apparent.

In anemic cases it is not necessary to bring the red-cell volume to normal before determining the fragility of the erythrocytes if the method used in estimating the percentage of the cells hemolyzed by the various concentrations of saline solution is sufficiently accurate. The fragility test as adapted by Hunter[4] to the photoelectric colorimeter meets this requirement. A minor modification of this method was made to save time. Constant and reliable values could be obtained by mixing the various dilutions of saline solution with blood in Klett–Summerson colorimeter tubes, centrifuging at 3000 r.p.m. for twenty minutes and measuring directly the amounts of hemoglobin in these tubes without decanting the supernatant into other tubes. No ammonium hydroxide was added.

Diagnosis of Congenital and Acquired Hemolytic Jaundice

The natural history of classic congenital hemolytic jaundice is well known. Typically there are episodes of anemia, acholuric jaundice, notable splenic enlargement and upper-abdominal pain from cholelithiasis. Whereas the symptoms tend to appear and disappear, the following signs persist throughout: microspherocytosis with increased fragility of the erythrocytes in hypotonic saline solutions, accompanied by anemia, reticulocytosis and increased urobilinogen content of feces. The disease frequently manifests itself in childhood or early adulthood, but may never be detected. Although the past history and family history may not reveal the presence of any of these features, blood studies of relatives of patients with this disease frequently demonstrate increased fragility, which is inherited as a mendelian dominant.[6] Many cases remain entirely asymptomatic throughout life; a few develop in older age groups. This work indicates that a case of hemolytic jaundice should not be termed congenital until evidence is found in the family of characteristic symptomatology or of microspherocytosis or increased red-cell fragility. The discovery of any or all of these characteristics in the blood is not enough to make the diagnosis certain. Meulengracht, cited by Dameshek and Schwartz,[7] denied that increased saline fragility was pathognomonic of congenital icterus, and reported cases of the acquired type with increased fragility. Furthermore, he stated that an inherited disturbance in formation was only one of the causes of increased fragility of the erythrocytes, and that actually the increase might be regarded as a regeneration phenomenon or as a sign of the action of toxic or hemolytic forces on the red cells in the circulation. Ham and Castle[8] comment on the effect of erythrostasis in the spleen and other organs to increase erythrocyte fragility in presumably otherwise normal persons. They report on the transient but striking increase in fragility that occurred in 5 cases of severe acute hemolytic anemia observed following the administration of sulfanilamide. This was so great that some of the red cells in venous samples were hemolyzed in isotonic or only slightly hypotonic saline solution. These authors believe that erythrostasis occurring in the spleen and other organs was "presumably operative" in bringing about the increased fragility. Watson[9] refers to 2 cases classified as macrocytic hemolytic anemia in association with liver disease that exhibited decreased resistance of the erythrocytes to hypotonic saline solution, without spherocytosis. These data demonstrate the difficulty in determining the fundamental nature of a hemolytic jaundice from fragility studies alone.

Singer and Dameshek[10] report a series of cases of so-called "symptomatic" hemolytic anemia, occurring in conjunction with other diseases (dermoid cyst in the ovary, chronic lymphatic leukemia, Hodgkin's disease, lymphosarcoma, severe liver disease and pneumonia with a panagglutinin). In these cases spherocytosis and increased hypotonic saline-solution fragility were frequently present. In the case associated with dermoid cyst in the ovary, splenectomy had a transient effect on the hemolytic jaundice, but removal of the tumor itself was marked by general improvement, subsidence of spherocytosis and a return of erythrocyte fragility to normal. Haden[11] also states that spherocytosis may occur in hemolytic anemia other than congenital hemolytic jaundice, reporting that it may be the result of leukemia, Hodgkin's disease or acetylphenylhydrazine poisoning. All these data indicate that a diagnosis of congenital hemolytic jaundice may not be made solely on the basis of laboratory findings in the blood of the patient.

In the case described we were not able to make a diagnosis, either preoperatively or postoperatively, of hemolytic jaundice of proved congenital origin. The most cogent points that argued against the congenital type were three in number. First, the history was not typical of the congenital form, with the sudden appearance of severe hemolytic anemia in old age. Second, there was no history among the patient's relatives of any condition resembling hemolytic jaundice, and the available relatives gave no laboratory evidence of the hematologic characteristics of this disease. Finally, the microscopic examination of the spleen was not characteristic of congenital hemolytic jaundice.[12] The pulp was only moderately filled with erythrocytes; the malpighian corpuscles were not obscured; and there was present an abnormal degree of phagocytosis. Therefore, the diagnosis made was relatively acute hemolytic anemia of the acquired variety. Since this diagnosis was made by exclusion, we cannot be certain that

our case was of the acquired variety any more than a disease can be called "acquired" unless a definite etiology can be established. It is concluded, however, on the basis of the data outlined above that the probability of its being acquired is great.

Acquired hemolytic anemia represents a heterogeneous group of cases, and may be broken down, for purposes of classification and therapy, into two subdivisions: those of known etiology and those whose etiology is unknown. Among the known causes are poisoning with such drugs as sulfanilamide,[8] acetylphenylhydrazine[11] and others. Also, this syndrome may occur in conjunction with other diseases, notably lymphomatous neoplasia.[10, 11] Still other cases occur without any pathologic accompaniment. As has been stressed above, increased erythrocyte fragility and microspherocytosis may be found in any of these types of acquired hemolytic jaundice, although less constantly than in the congenital form.

Splenectomy for Acquired Hemolytic Jaundice in the Aged

Splenectomy is attended by greatly increased risk when performed, for whatever reason, on aged persons.[7] This fact, together with the distinct possibility that the removal of the spleen might well have no remedial effect on this patient's acquired hemolytic jaundice, made it seem advisable to try all other reasonable therapeutic measures first. Intensive liver and iron therapy, intensive transfusion therapy (which was marked by an increasing frequency of reactions) and roentgen-ray therapy directed at the trunk, however, were ineffective or of no permanent benefit. Splenectomy, on the other hand, proved effective.

Subsequent study of the literature revealed 15 patients, including the one here reported, in whom the onset of hemolytic jaundice occurred at or beyond the age of fifty, and in whom not all the essential criteria for a diagnosis of congenital hemolytic jaundice, as discussed above, were present. About half these were patients in their fifties. Two had passed their seventieth birthday at the time of onset, the patient here described being seventy and another being seventy-five. The family and past histories were noncontributory. Symptoms and physical signs — which were of no differential diagnostic or prognostic import — included loss of energy, anorexia, weakness, palpitation, shortness of breath on exertion, pallor, jaundice and enlargement of the liver and, somewhat more regularly, of the spleen.

Of the 15 cases, 5 showed definite improvement

TABLE 1. *Splenectomy Resulting in Definite Improvement.*

CASE NO.	SOURCE	AGE AT ONSET	RED-CELL FRAGILITY	SPHEROCYTOSIS	RESULTS OF SPLENECTOMY	PATHOLOGICAL REPORT ON SPLEEN
1	Mandelbaum[5]	75	Normal at onset; later increased preoperatively and postoperatively.	Present	Slow but steady improvement	Weight, 650 gm.; thickened trabeculae; reticuloendothelial elements increased; sinuses distended and lining cells prominent; much extracellular and intracellular iron-containing pigment.
2	Israëls and Wilkinson[13] (Case 2)	57	Increased	Present	Slow but steady improvement	Weight, 700 gm.; no increase in connective tissue; sinuses dilated, histiocytes remarkably prominent in pulp; erythrocytes very scanty.
3	Davidson and Fullerton[14] (Case 6)	60	Normal	Absent	Good recovery; during bronchitis 4 years later the patient was mildly jaundiced.	Malpighian corpuscles smaller than usual and widely separated owing to an increase in pulp, which was due to an excessive number of red cells; findings consistent with usual findings in acholuric jaundice.
4	East[15]	52	Normal preoperatively; slightly increased postoperatively.	Not mentioned	Slow but steady improvement	Weight, 600 gm.; normal malpighian corpuscles; hyperplastic endothelium, whose cells contained large iron-bearing granules; phagocytosis of red cells and occasional giant cells.
5	James and Evans	70	Normal by ordinary methods; increased if corrected for anemia, preoperatively and postoperatively.	Absent	Good recovery	Weight 362 gm.; marked hematopoiesis with extensive hemosiderin deposits both within and without cells; normal malpighian corpuscles.

after splenectomy. These 5 cases comprised the 2 over seventy years of age, 1 in the sixties and 2 in the fifties. The essential data are summarized in Table 1. It is interesting to note that in only 1 of these cases (Case 3) was there a pathologic picture like that seen in congenital hemolytic jaundice. In this case fragility of the red cells was said to be normal, and spherocytosis was not mentioned. In the other spleens a marked increase in the number and activity of reticuloendothelial elements was found.

In 10 of the cases reported in the literature splenectomy was ineffective or resulted in acceleration of the downhill course. Of these, 6 are summarized in sufficient detail to make an analysis valuable (Table 2). It will be noted that in but 1 of these cases (Case 5) did the spleen show a microscopic picture like that of congenital hemolytic jaundice. This patient died of obvious congestive heart failure thirty-six hours postoperatively. It is probable that there was not time for the effect of splenectomy to be demonstrated. The remaining 4 cases, which are not included in Table 2, were reported by Dameshek and Schwartz[7] and are those of acute acquired hemolytic anemia in all of which operative death occurred. The ages in these cases ranged from fifty to sixty-four.

In 6 of these 10 cases, the primary cause of death was found to be closely related to the operative procedure, whereas in 3 the blood dyscrasia itself was the principal lethal agent. One patient died six weeks after operation, and autopsy did not help to make a diagnosis. Presumably this death also was related to the hemolytic process.

The question arises whether cases with increased erythrocyte fragility have a better prognosis than do those with normal fragility. In the group of 5 cases showing improvement after splenectomy, 2 showed increased fragility preoperatively. In 2 others the fragility, although reported as normal before operation, increased after recovery. It is probable that in the studies made before operation the presence of anemia masked the increased fragility of the erythrocytes. In the group of 6 cases analyzed in which splenectomy failed to result in improvement, 3 showed increased erythrocyte fragility. It is impossible to say how many more of these might have manifested increased fragility had more accurate methods been used.

The cases reviewed from the literature, as well as the one reported here, demonstrate that splenectomy may save the lives of elderly patients with acquired hemolytic jaundice, and that it should not be regarded as a useless procedure. Although good results following splenectomy are likelier in a patient with increased erythrocyte fragility, spherocytosis and a spleen typical of congenital hemolytic jaundice than they are in others, it is sometimes of value in patients whose clinical picture lacks one or more of these characteristics.

TABLE 2. *Splenectomy Without Improvement.*

Case No.	Source	Age at Onset	Red-Cell Fragility*	Results of Splenectomy	Pathological Report on Spleen
1	Watson[9] (Case 74)	67	Increased	Atelectasis and death on 3rd postoperative day	Weight, 880 gm.; sinuses markedly dilated.†
2	Davidson and Fullerton[14] (Case 9)	51	Normal	Blood count progressively decreased with death 10 days postoperatively	Weight, 815 gm.; marked proliferation and activity of reticuloendothelial system; definite myeloid metaplasia; findings said to be "typical of reticuloendotheliosis."
3	Thompson[16] (Case 33)	63	Normal	Death 6 wk. postoperatively; autopsy no aid in diagnosis.	Weight, 680 gm.; evidence of marked blood formation.
4	Davidson[17] (Case 5)	55	Normal	Reticulocytosis persisted; death 10 mo. later of anemia.	Weight, 1700 gm.; histiocyte proliferation and myeloid metaplasia; characteristics of congenital hemolytic jaundice absent.
5	Davidson[17] (Case 9)	58	Increased	Congestive heart failure 36 hr. postoperatively; red-cell count 470,000 at time of death.	Weight, 820 gm.; pulp contained innumerable red cells without marked dilatation of sinuses; the appearances were said to be "those of acholuric jaundice."
6	Rastetter and Murphy[18] (Case 2)	53	Slightly increased	Icterus, anemia and reticulocytosis returned after 1 mo. improvement; death 2 wk. later.	Weight, 560 gm.; section showed dark-red pulp with faintly visible follicles; marked congestion of sinuses; reticulum cells scant.

*No spherocytes were found in any of the cases listed in this table.
†This patient also had hepatic cirrhosis.

Summary

A case of severe acquired hemolytic jaundice with onset at the age of seventy, apparently cured by splenectomy, is presented.

The technic of determination of erythrocyte fragility is discussed. The shortcomings of widely used methods are pointed out, and the advantages

of recent improvements devised by various workers are described.

The differential diagnosis of hemolytic jaundice is discussed, with special reference to the diagnostic import of abnormally fragile red cells and of microspherocytosis.

From the literature are reported 14 other cases of acquired hemolytic jaundice, with onset after the age of fifty in which splenectomy was performed. Factors influencing the course of these cases are presented.

References

1. Todd, J. C., and Sanford, A. H. *Clinical Diagnosis by Laboratory Methods: A working manual of clinical pathology*. Ninth edition. 841 pp. Philadelphia: W. B. Saunders Company, 1939. P. 320.
2. Daland, G. A., and Worthley, K. Resistance of red blood cells to hemolysis in hypotonic solutions of sodium chloride: observations in blood disorders. *J. Lab. & Clin. Med.* **20**:1122-1136, 1935.
3. Ham, T. H. Studies on destruction of red blood cells: chronic hemolytic anemia with paroxysmal nocturnal hemoglobinuria: investigation of mechanism of hemolysis, with observations on five cases. *Arch. Int. Med.* **64**:1271-1305, 1939.
4. Hunter, F. T. Photoelectric method for quantitative determination of erythrocyte fragility. *J. Clin. Investigation* **19**:691-694, 1940.
5. Mandelbaum, H. Congenital hemolytic jaundice: report of case of congenital hemolytic jaundice: initial hemolytic crisis occurring at age of 75: splenectomy followed by recovery. *Ann. Int. Med.* **13**:872-883, 1939.
6. Campbell, J. M. H., and Warner, E. C. Heredity in acholuric jaundice. *Quart. J. Med.* **19**:333-355, 1926.
7. Dameshek, W., and Schwartz, S. O. Acute hemolytic anemia (acquired hemolytic icterus, acute type). *Medicine* **19**:231-327, 1940.
8. Ham, T. H., and Castle, W. B. Relation of increased hypotonic fragility and of erythrostasis to mechanism of hemolysis in certain anemias. *Tr. A. Am. Physicians* **55**:127-132, 1940.
9. Watson, C. J. Hemolytic jaundice and macrocytic hemolytic anemia: certain observations in series of thirty-five cases. *Ann. Int. Med.* **12**:1782-1796, 1939.
10. Singer, K., and Dameshek, W. Symptomatic hemolytic anemia. *Ann. Int. Med.* **15**:544-563, 1941.
11. Haden, R. L. *Studies in Hematology*. Porter Lectures, Series X. 86 pp. Lawrence, Kansas: University Extension Division, University of Kansas, 1940.
12. Thompson, W. P. Splenic lesion in hemolytic jaundice. *Bull. Johns Hopkins Hosp.* **51**:365-370, 1932.
13. Israëls, M. C. G., and Wilkinson, J. F. Haemolytic (spherocytic) jaundice in adults. *Quart. J. Med.* **31**(N.S. 7): 137-150, 1938.
14. Davidson, L. S. P., and Fullerton, H. W. Some rare types of macrocytic anaemia. *Quart. J. Med.* **31**(N.S. 7): 43-84, 1938.
15. East, T. Acholuric jaundice with almost normal erythrocyte fragility. *Proc. Roy. Soc. Med.* **26**:365, 1933.
16. Thompson, W. P. Hemolytic jaundice: its diagnosis, behavior and treatment: review of 45 cases. *J. A. M. A.* **107**:1776-1781, 1936.
17. Davidson, L. S. P. Macrocytic haemolytic anaemia. *Quart. J Med.* **25**(N.S. 1): 543-578, 1932.
18. Rastetter, J. W., and Murphy, F. D. Acquired hemolytic jaundice. *Am. J. Digest. Dis. & Nutrition* **4**:805-810, 1938.

THE DEVELOPMENT OF THE STATE CHILD-GUIDANCE CLINICS IN MASSACHUSETTS*

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THE Commonwealth of Massachusetts was the first state to provide by legislation (in 1922) for a division of mental hygiene,[1] with the establishment of child-guidance clinics financed by state funds as one of its major activities. A review of the diversely related developments in psychiatric therapy that culminated in the child-guidance movement shows the state guidance clinics emerging at the peak of the mental-hygiene movement as the logical but unforeseen outcome of efforts to promote mental health by preventive and early correctional treatment.

The mental-hygiene movement expanded with remarkable rapidity through the years 1912 to 1922 under the impact of new psychiatric concepts of mental disease and an increasing revelation of the importance of flaws of personality in precipitating breakdowns in adult life.

A concurrent stimulus was contributed through the adoption by mental hospitals of social services, which brought to light many pertinent aspects of life experiences of patients by means of investigations in the homes and collaboration with local agencies. This type of social service rapidly developed into a specialized profession forming a connecting link between the hospitals and the communities that they served, and providing a valuable medium for the interpretation of the principles of mental hygiene to the lay public. By 1922, Massachusetts was considered a leader in the new field of psychiatric social service, and trained workers were in great demand by other states.[2] This expansion of community services was facilitated by the establishment of outpatient clinics for supervision of released patients. These clinics soon became centers for treatment of noncommittable patients, among whom were some children, chiefly delinquents.

In 1919, the General Court of Massachusetts made obligatory the examination of all school children who were three-years retarded, and the formation of special classes where ten or more such children were found.[3] The examining service was provided by the state hospitals and the Walter E. Fernald State School (for the feeble-minded) by means of clinics distributed through the Commonwealth and called "traveling school clinics." The impetus that this procedure gave in the direction of child guidance was incalculable and proved to be a most notable contribution to the program of mental hygiene. Although the service was at first viewed by school boards with suspicion and fear of increased expense for special classes, it quickly demonstrated its value, and schools began to refer

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many children whose difficulties proved to be due not to mental deficiency but to physical or environmental handicaps.

By 1920, in addition to the traveling school clinics, a number of outpatient mental-hygiene clinics were well established, giving service to adults and children. Northampton had four clinics, and Gardner three. In 1921, Monson had four, Danvers seven, and Taunton two, and Worcester had opened such a clinic at the Summer Street Department.[4] At that time, the Boston Psychopathic Hospital was established as an independent unit for screening of committable cases and furnishing treatment for milder forms of mental illness. The latter service was in immediate demand and was faced with problems from infancy to adulthood.[5]

By acts of 1921 and 1924, the Division for the Examination of Prisoners was established and financed by the Commonwealth, and was completely equipped with psychiatric and social services.

The case histories in all these different fields presented striking similarities of etiologic factors and unmistakable indications that the most fertile field for mental hygiene lay in the realm of childhood. Meanwhile sporadic experiments in specialized clinics for children were being made throughout the country, chiefly directed toward the treatment of delinquency. In 1922, a series of demonstration clinics was planned by the National Committee for Mental Hygiene through its Division for the Prevention of Delinquency. This was financed by the Commonwealth Fund on a five-year plan, and the clinics were located in eight specially selected cities. Of these eight clinics, four survived the exigencies of pioneering, another was subsequently resuscitated, and another was reorganized by two communities, resulting in seven established clinics. The chief problem was the continued financing after termination of the demonstration period. Results of therapy with adjudged delinquents were discouraging, but again the signposts pointed toward earlier recognition and treatment of maladjusted children.[6]

In this preliminary period, prior to 1922, one phase of clinical procedure was worked out that has remained standard to date, namely, the professional clinic team of psychiatrist, psychologist and psychiatric social worker. Although many variations of responsibility have been used, in actual practice each has been found to have its indispensable contribution toward the evaluation and treatment of cases, and the combination has proved more effectual than the efforts of any one type of worker.

In Boston, in November, 1921, Dr. Douglas A. Thom was asked to make a survey of one of the health clinics of the Baby Hygiene Association of Boston to determine whether a psychiatrist might have something to contribute to the clinics' program of preventive medicine.[7] From misgivings concerning the possibility of accomplishing anything with these immature patients, Dr. Thom was quickly converted to enthusiasm for the rich field of opportunity that opened before him.[8] Soon three clinics for young children were put in operation under his direction by the Community Health Association (visiting nurses), and were called "habit clinics" as an innocuous but descriptive name. These seemed to be the first clinics in the country that were established specifically for psychiatric therapy for young children.[9] With startling clearness, the social evils of poverty, disease, ignorance and vice came into focus as the ravagers of childhood and the breeding ground of mental disease.

In 1922, Dr. George M. Kline, with Dr. Thom and other leading psychiatrists, spurred on by the ominous crowding of the state hospitals, presented to the Legislature a preventive program and secured the establishment of the Division of Mental Hygiene, under the Department of Mental Health, with Dr. Thom as director. The division was charged with the responsibility for "all matters affecting the mental health of citizens of the Commonwealth, investigation of causes and conditions that tend to jeopardize mental health."[10] State funds were appropriated for research and for children's clinics.

In 1923, three clinics* were opened in Boston by the Division of Mental Hygiene and were promptly utilized by children's agencies, visiting nurses and family-welfare workers. In this year also, the Worcester State Hospital established a habit clinic for children such as had previously been seen at its Psychiatric Clinic.[11] This clinic was later discontinued and the children were seen at the Memorial Hospital.[12] In 1924, four additional clinics were started by the division.† The clinic in the West End (Boston) is still flourishing, having given twenty years of service to a wide area. Two years later the Lynn Clinic was transferred to the auspices of the Danvers State Hospital in order that the clinic staff of the division might be available for a new clinic at Quincy. The Springfield Clinic, which was started as a demonstration clinic because of its distance from Boston, was assisted by private agencies after one year of operation and received general supervision from the Monson State Hospital.[13]

The initial work of projecting clinics in new communities was undertaken jointly by the division and the Massachusetts Society for Mental Hygiene,[14] which has carried on an aggressive and effective program since the beginning of the movement.

*The first of these was established on June 6, at the Maverick Dispensary, East Boston. It was transferred to the auspices of the Boston Psychopathic Hospital on July 2, 1924. The second was begun on June 8, 1923 at the North End (Boston) Health Unit. It was closed in July, 1928, and reopened in October, 1928, at the North Bennet Street Industrial School. It was consolidated with the West End Clinic in October, 1929. The third was established on October 25, 1923, at the Roxbury Neighborhood House, and was closed on September 18, 1924.

†The first was opened on January 12, 1924, at the West End Health Unit, West End (Boston); the second on March 5, 1924 at the Lynn General Hospital (transferred to the Danvers State Hospital on March 30, 1926); the third on April 25, 1924, at the Lawrence General Hospital (transferred to the Danvers State Hospital on March 5, 1940); and the fourth on October 24, 1924, at Springfield (transferred to the supervision of the Monson State Hospital on October 31, 1925, and reorganized with community support on November 20, 1938).

Opportunities were sought for talks and conferences, and when sufficient interest was aroused a sponsoring group was organized to promote publicity, find accommodations and consult with the clinic team on community problems. Theoretically, all the clinics set up by the division were for demonstration, and were eventually to be turned over to hospitals or private organizations. This plan has been carried out except in communities easily available from Boston.

In 1925, four more clinics were in operation.* The clinic at the Boston Dispensary became a part of the Children's Department of this hospital, and in 1933 service was extended to two sessions weekly and the clinic provided training in child therapy for medical interns. The Lowell Clinic also started in a local general hospital, but after two years gave over its patients to a private clinic in the community. Four years later, at the request of schools and agencies, it was reopened and has continued service to date. The Reading Clinic was opened as a monthly diagnostic service for the school department, and in 1931 service was extended to weekly sessions for child guidance and treatment. After a period of full activity conditions changed, and it was closed in 1939 because of decreasing community interest and pressing demands for service by the City of Brockton. The Beverly Clinic also gave diagnostic service until 1931, when it became well established as a weekly guidance clinic. It was taken over by the Danvers State Hospital in 1932.

The Out-Patient Department of the Worcester State Hospital was reorganized during 1925[15] to provide more specialized treatment for children attending the Psychiatric Clinic at the Memorial Hospital.

Already various patterns were emerging among these pioneer clinics. Demonstration clinics had been taken over by the staffs of the state hospitals, communities had rallied to financial support to obtain increased service, clinics housed in hospitals had begun to function as training centers, schools had begun to use clinics for the solution of problems, and contacts with children had contributed valuable information to psychiatrists. The child-guidance movement had won prestige both in professional and in popular esteem.

In 1926, the division started the Quincy Clinic,† which proved to be one of the most successful and is still in the process of expansion. It serves a wide circle of surrounding towns and receives a large percentage of its cases from public schools. For a few years, it attempted to meet the pressure by using a double staff, then increased service to two sessions weekly in January, 1943, and is now in the process of obtaining community funds for enlarged scope through the interest of a local sponsoring committee.

In Worcester a clinic for children was organized[16] during this year under the name of the Child Guidance Clinic and embarked on its eminently successful career. In the following two years, community interest and support increased so that in 1929 it was able to offer full-time service with the financial participation of the Child Guidance Association of Worcester.[17]

At that time, the traveling school clinics began to be under continual pressure to furnish treatment as well as diagnostic service to children who were not defective but who were in need of help, and many cases of this type were served.[18]

The year 1927 saw eight clinics of the division and five clinics of the state hospitals well under way. Methods used in Massachusetts were being studied and adopted by other states and other countries.[19] Inquiring visitors were frequent. Schools of social work had co-operated since 1923 in offering related courses and were sending students to the clinics for field training. Social workers were eager to enter the field, but the demand for trained personnel far exceeded the supply.

During 1927, the Taunton State Hospital opened a clinic at the hospital and also one for adults and children at the Sturdy Memorial Hospital in Attleboro.

On December 1, 1927, the Habit Clinic at the New England Hospital for Women and Children in Roxbury, which had previously been conducted under private auspices by Dr. Thom came under the jurisdiction of the division. This clinic worked in co-operation with the hospital and served a large residential district in the southern section of Boston. It was chiefly a treatment clinic, holding one session weekly and maintaining quite steadily an average attendance of 10 cases per session over a period of sixteen years, until it was consolidated with the Southard Clinic in October, 1943.

In July, 1928, a new venture was initiated in giving clinic service monthly to tuberculous children at the North Reading Sanatorium. A careful survey was made for the purpose of improving educational facilities, resulting in the introduction of occupational therapy. Considerable social case work was done in co-operation with the Department of Public Health. Owing to the pressure of work in community clinics, this service was changed in 1939 to a consultation service on call.

In October, 1929, the division organized another community clinic in Norwood, sponsored but not financed by an active group of social-minded women. It was housed at the Norwood Hospital and served towns and rural districts to the south and west of

*One of these was opened at the Boston Dispensary on December 5, 1924, and was consolidated with the Southard Clinic at the Boston Psychopathic Hospital in October, 1943. The second was established on December 3, 1924, at St. John's Hospital, Lowell, and was closed in 1927. It was reopened at the School Clinic Building on January 22, 1932, and was moved to Lowell General Hospital in 1933. The third was opened in December, 1924, at the Town Hall, Reading, and closed on September 30, 1939. The fourth was opened on March 12, 1925 at the Beverly Health Center, and was transferred to the Danvers State Hospital on April 13, 1932.

†It was opened on October 7, 1926, at the Quincy Dispensary, was conducted at the Woodward School from 1931 to 1943, and has been at the Children's Health Center since 1943.

Boston, and was well patronized by school principals and nurses. Restrictions of transportation in 1943 necessitated the closing of this clinic in October, and its cases were referred to the Southard Clinic in Boston.

The years 1929, 1930, 1931 and 1932 were significant in the establishment of ten state-hospital clinics.* The Fall River Clinic was a general psychiatric clinic until 1940, when it became a child-guidance clinic. These clinics, with the exception of Quincy, have continued to function on a weekly or monthly basis. The Quincy Clinic undertook the treatment of court cases and adolescents who were above age for the clinic conducted by the division in Quincy. After February, 1943, services were rendered only on call from the court or schools, and treatment cases were referred to the Division Clinic, which had for some time been accepting adolescents as well as younger children.

It had been the ambition of the division to have clinical facilities accessible to all citizens of the Commonwealth, but up to that time services had concentrated in the more populous eastern section. In May and June, 1931, demonstration clinics were instituted in Northampton and Holyoke and, following the six-month demonstration period, they were transferred to the auspices of the Northampton State Hospital in December, 1931.

In the year 1932, the division reopened the clinic at Lowell. This was a new type of co-operative venture undertaken at the request of the school department, which felt the need of a special school survey and the instruction of teachers in the principles of mental hygiene. The clinic was later moved to the Lowell General Hospital, and has changed in character because of its association with the hospital and its less central location. At the time of this resumption of responsibility, the Danvers State Hospital took over from the division the well established clinic at Beverly. In October of the following year, the Danvers State Hospital opened a clinic at the Community Health Center in Newburyport.

The year 1933 rounded out ten years of service of the state child-guidance clinics,[20] and various trends were in evidence. The original intention of the division to turn over its demonstration clinics to state hospitals as psychiatric centers of their respective districts had been carried out in six instances, and the hospitals had initiated clinics of their own in eight communities. The division itself was conducting nine clinics, which were acquiring an aspect of permanence. Five of these were so-called "community clinics," affiliated more closely with schools and social agencies than with medical centers. Advantages were apparent in each type. The community clinics had become a part of community life, and were influential in the education of teachers through school conferences and in the education of parents through mothers' clubs and parent-teacher associations. The emphasis was on the problems of the normal child. The social and economic level of the patients was somewhat higher than that in the clinics that were affiliated with hospitals. The latter had advantages of medical services whenever needed and had a somewhat larger proportion of serious cases. These clinics also furnished an opportunity for instruction of medical interns and student nurses in the recognition and treatment of neurotic symptoms.

This period saw the beginning of special services in the clinics, such as speech correction, remedial reading and occupational therapy.

During these first ten years, the division had registered 5043 cases, which furnished a basis for analysis and research. Special studies and published articles by clinic personnel had become a part of the campaign for mental health.

The pressure of applications for intake necessitated the formulation of selective criteria for acceptance of cases suitable for clinic therapy, but the fact that the service was free under state support placed the clinics under obligation to accept maximum loads. This condition produced in an aggravated form the same dilemma that beset the generously staffed demonstration clinics of the Commonwealth Fund[21] — the question whether to give intensive therapy to a few or more generalized treatment to many. Psychoanalytic procedure was impossible under the circumstances and would have met with popular prejudice; in fact, it was indicated in only a few cases that could be referred to private agencies, such as the Judge Baker Foundation, the New England Home for Little Wanderers and the Psychiatric Clinic of the Massachusetts General Hospital. Psychiatrists trained under various schools of thought directed their efforts toward improving parental attitudes and modifying the personal problems of children. In some cases the mother needed therapy as much as the child, and the social workers began to undertake this responsibility under the direction of the psychiatrists. The year-by-year discussions of all these problems in reports and bulletins give a dramatic picture of a pioneering effort with successes and failures but always unfailing enthusiasm.[22]

The last ten years, from 1933 to 1943, have constituted a period of stabilization rather than of expansion. The division had reached the financial saturation point and could establish new clinics only by closing its less effective ones. Some new state

*These were as follows: Quincy, November, 1929, auspices of Medfield State Hospital, at Quincy School Annex (closed February, 1943); Fall River, 1930, auspices of Taunton State Hospital, at City Hall Annex; Norwood, 1930, auspices of Medfield State Hospital, at Norwood Hospital (closed June, 1935); Gardner, July, 1930, auspices of Gardner State Hospital, at Gardner High School; Fitchburg, July, 1930, auspices of Gardner State Hospital, at Academy Street School; Haverhill, January, 1931, auspices of Danvers State Hospital, at Haverhill High School (closed February, 1944); Lawrence, January, 1931, auspices of Danvers State Hospital, at International Institute; Gloucester, January, 1932, auspices of Danvers State Hospital, at Hovey School (closed June, 1934); Warwick, 1931, auspices of Gardner State Hospital, at Central School; and Athol, October, 1931, auspices of Gardner State Hospital, at Red Cross Headquarters.

hospital clinics were started.* The Salem Clinic has made a valuable contribution; the Waltham Clinic was doing intensive and effective work when it was closed for lack of personnel; the Amherst and Greenfield clinics served a hitherto neglected area.

In 1938, the Springfield Clinic expanded into a full-time clinic with financial contribution from the Community Chest. The school department furnished excellent quarters, and a sponsoring group formed the Guidance Clinic Association, which has acted in the capacity of an advisory board of directors.

The chief innovation of the division was the establishment of a clinic in Brockton on September 30, 1938, in co-operation with the school department, which has provided housing and stenographic service. In October, 1939, it expanded to two sessions weekly and still has an extremely heavy case load, obviously needing more service. This clinic exemplifies the type of clinic that can be developed through an intelligent educational policy to reach children of all ages. The clinic offers special services for speech correction, remedial reading and occupational therapy. Special classes for superior children have been in operation in the school system, with close supervision from the clinic. Brockton has an effective group of social agencies that co-operate with the Guidance Clinic both in case work and in a community program for mental health.

The division opened trial clinics in Hamilton (1940–1941) and Marblehead (1940–1942), which were discontinued because of lack of referrals by the communities. The Barnstable Clinic, opened in September, 1942, is developing as a mental-hygiene center for southeastern Massachusetts and Cape Cod, holding four sessions monthly at the Hyannis Town Hall.

The Quincy Clinic, which is a school and community clinic, has outgrown its original setup. In January, 1943, it added a second weekly session, and in December, 1943, moved to quarters in the Child Health Center. Community interest has resulted in the formation of the Guidance Association, which has obtained supplementary financial support for enlarged services. The Guidance Association is a member of the Quincy Council of Social Agencies, which is extremely active and promotes efficient social work in the city.

The new Southard Clinic, opened in Boston in 1943, is a different type of clinic and contemplates an extension of service for which the division has been clamoring for ten years. This clinic is a consolidation of the children's work of the Out-Patient Department of the Boston Psychopathic Hospital with three division clinics that were discontinued to provide personnel. It is housed at the Boston Psychopathic Hospital and has the advantage of access to the specialized facilities of the institution for the diagnosis and treatment of serious cases. A definite disadvantage is found in the objection of many parents to any contact with a mental hospital, especially one that is stigmatized with the prefix "psycho-." This troublesome problem could be met by the erection of a separate building that would furnish headquarters for the Division of Mental Hygiene and the Division of Mental Deficiency, and would have a ward for the observation and treatment of young psychotic patients. Massachusetts has lagged behind other states in its failure to provide for segregation of such patients, who at present must mingle in the wards of mental hospitals with adult patients, an environment that is extremely detrimental to recovery.[23]

The changes that have taken place in the last ten years have been in the direction of stabilization and efficiency. On January 1, 1944, nearly 12,000 cases had been accepted by the division clinics (exclusive of Springfield and Worcester) for diagnosis and therapy. The pressure of quantity has caused emphasis to be laid on essentials, economy of effort and selectivity of service. Co-operative resources have been utilized with mutual benefit. Student training has kept social workers up to date in methods of social therapy and has provided the clinics with assistance in case work. Special services in speech and reading, as well as hobby classes, have enhanced the value of the clinics. The constructive aim of helping children to attain a normal emotional maturity has been contagious and inspiring.

Twenty years of experiment and demonstration could not have been carried out on so large a scale without state financing. This provided security, minimized the effect of incidental failures, allowed changes of location and exchanges of responsibility between hospitals and the division, and made possible a statewide program for mental health. The benefits of such assistance outweigh the burdens and restrictions that are implicit in a state-supported service.

Much credit for the success of the child-guidance movement must be attributed to the gifted and forward-looking psychiatrists who initiated it and carried it on.

*These were as follows: Salem, 1934, under auspices of Danvers State Hospital, at Pinkham Memorial Building; Melrose, 1934, under auspices of Danvers State Hospital, at Calvin Coolidge School (closed June, 1937); Waltham, May, 1936, under auspices of Metropolitan State Hospital, at the hospital (closed, 1941); Amherst, November, 1939, under auspices of Northampton State Hospital, at Amherst Town Hall (closed June, 1943); Greenfield, 1942, under auspices of Northampton State Hospital, at Domestic Science Cottage; and New Bedford, November, 1923, under auspices of Taunton State Hospital (originally intended as a general psychiatric clinic for adults and children but in 1940 changed to a child-guidance clinic).

References

1. *Acts and Resolves of Massachusetts.* Chapter 519. Boston: Wright & Potter Printing Company, 1922. P. 631.
2. *Annual Report of the Massachusetts Department of Mental Diseases.* 1920: pp. 49-56.
3. *Acts and Resolves of Massachusetts.* Chapter 277. Boston: Wright & Potter Printing Company, 1919. P. 222.
4. Caldicott, G. F. Preliminary report of mental clinic of Worcester State Hospital. *Boston M. & S. J.* **186**:568-572, 1922.
5. *Annual Report of the Massachusetts Department of Mental Diseases.* 1920: pp. 85 and 86.

6. Stevenson, G. S. *Child Guidance Clinics: A quarter century of development.* 186 pp. New York: Commonwealth Fund, 1934.
7. *Children's Bureau Publication.* No. 135. Washington, D. C.: Government Printing Office, 1924.
8. Habit clinics for children of pre-school age. *Ment. Hyg.* 6:463, 1922.
9. *Proceedings of the First International Congress on Mental Hygiene, 1932.* Vol. 2: p. 755.
10. *Annual Report of the Massachusetts Department of Mental Diseases.* 1922: p. 7.
11. *Annual Report of the Worcester State Hospital, 1923:* p. 11. 1924: p. 8.
12. *Annual Report of the Massachusetts Department of Mental Diseases.* 1924: p. 43.
13. *Annual Report of the Massachusetts Department of Mental Diseases.* 1925: p. 31.
14. *Bulletin of the Massachusetts Department of Mental Diseases.* April, 1924: pp. 2-4.
15. *Annual Report of the Massachusetts Department of Mental Diseases.* 1925: p. 45.
16. *Annual Report of the Worcester State Hospital.* 1926: pp. 11 and 12.
17. *Annual Report of the Worcester State Hospital.* 1927: p. 15. 1928: p. 13. 1929: pp. 22 and 23.
18. *Annual Report of the Massachusetts Department of Mental Diseases.* 1926: pp. 54 and 64.
19. *Annual Report of the Massachusetts Department of Mental Diseases.* 1927: p. 20.
20. Hoskins, E. Ten years of social work in habit clinics of Division of Mental Hygiene. *Bull. Mass. Dept. Ment. Dis.* 18:37-46, 1934.
21. Stevenson.[8] Pp. 54-59.
22. Thom, D. A. Annual report of the Massachusetts Division of Mental Hygiene. In *Annual Report of the Massachusetts Department of Mental Diseases.* 1933: pp. 44-47 and 49-55. 1934: pp. 57-66.
23. Yerbury, E. C. State mental hygiene program. *Ment. Hyg.* 27: 457-468, 1943.

MEDICAL PROGRESS

MYCOTIC INFECTIONS*

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NUMEROUS medical problems have been created by sudden changes in the living habits of large groups of the population. Emigration to different localities, the influx of workers into industries with which they have had no previous contact and the grouping of thousands of men in camps, both in this country and abroad, have contributed to the shifting problems of health. Diseases heretofore restricted to or endemic in certain areas or peculiar to certain industries have appeared sporadically and at times with epidemic proportions in areas or industries where they had not previously been reported. It is now necessary, therefore, that the practicing physician constantly focus his attention on an increasing horizon of infectious diseases.

Among such diseases, the mycotic infections have gained great importance. Previous epidemics of so-called "athlete's foot" among civilian members of social, fraternal or athletic organizations, due to the widespread use of showers and swimming-pool facilities, have become overshadowed by the rate of infection and seriousness of this disease among the troops. Saffron[1] has reported fungus infection as one of the five diseases most frequently attacking the skin of fighting men, and estimates the incidence of infection in various groups to be as high as 40 to 90 per cent. Downing[2] has also reported on the increasing problem of fungus infections in various camps. According to Goldstein and Louie,[3] alarming numbers of American troops have acquired coccidioidomycosis while training in endemic areas in this country where *Coccidioides immitis* is known to occur in the soil. On return to civilian life, these patients will scatter to all sections of the country and will necessitate the inclusion of coccidioidomycosis in the differential diagnosis of pulmonary infections outside of areas where the disease is known to be endemic. From the few samples cited above, it can readily be seen that the medical profession must gain a better understanding of the prevention and control of fungus infections.

With the exception of a few endemic areas, the geographic distribution of fungus infections is worldwide. The distribution of such diseases depends in reality on their recognition alone, and their frequency of occurrence demands that they be considered in the differential diagnosis of any infection of the skin or internal organs. It is the purpose of this article to present a résumé of the field of medical mycology as an aid to those who are comparatively unfamiliar with the types of infection produced by fungi.

Fungus infections can be conveniently divided into four major categories: namely, superficial mycoses, dermatomycoses, subcutaneous mycoses and systemic mycoses. These will now be considered.

SUPERFICIAL MYCOSES

Included in the category of superficial mycoses are a few fungus diseases caused by a heterogeneous group of organisms, considered to be saprophytic species but occasionally producing superficial lesions on the skin or hair.

Tinea versicolor

Tinea versicolor is the most superficial of all the fungus diseases, with subjective symptoms lacking or with slight pruritus, the lesions involving usually the trunk but occasionally the neck, face, axillas and arms. The disease is characterized by a yellowish or brownish macular eruption and is caused by

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Malassezia furfur. Although cultures of this fungus have been obtained,[4, 5] the clinical diagnosis is confirmed by a microscopic examination of potassium hydroxide preparations of the furfuraceous scales covering the colored areas. In such preparations the fungus appears as clusters of round, thick-walled, budding forms intermixed with branching mycelial fragments. Treatment is directed toward the removal of the infected scales by daily hot, soapy baths, followed by an application of a 20 per cent aqueous solution of sodium hyposulfite.

Erythrasma

Erythrasma is a somewhat chronic superficial fungus infection confined to the skin of the axillary, pubic or genitocrural areas. The disease is characterized by sharply circumscribed maculopapular lesions having a reddish-yellow to reddish-brown pigmentation with overlying furfuraceous scales that feel greasy. The causative fungus, *Actinomyces* (*Nocardia*) *minutissima*, has been cultured but, as with tinea versicolor, the clinical diagnosis is confirmed by a microscopic examination of potassium hydroxide preparations of material scraped from the lesions. Such preparations reveal short, delicate, branching filaments 1 micron in diameter that are consistent in size with those seen in species of Actinomyces. The treatment is the same as that described for tinea versicolor.

Trichomycosis

Trichomycosis is an infection of the axillary or pubic hairs without involvement of the surrounding skin. The disease is characterized by lusterless, brittle hair with yellow, red or black concretions extending for some distance or occurring as isolated nodules along the hair shaft, and is caused by *Act. tenuis*. Chromogenic cocci mixed in the mucilaginous material composing the nodules are responsible for the red or black pigmentation of the colored varieties.[6] Microscopic preparations in potassium hydroxide reveal numerous cocci mixed with short, branching, thin mycelial fragments. Effective treatment involves shaving the hair and daily treatment with 3 per cent sulfur ointment or application of a 1:1000 solution of mercury bichloride.

Piedra

Piedra, a disease of the hair of the head or face, is known to occur in two varieties — black piedra, confined to the tropics and caused by *Piedraia hortai*,[7] and white piedra, occurring in the tropics and also in Europe, caused by *Trichosporon beigelii*.[8] The disease is characterized by black or light-colored, hard nodules adherent to the hair shaft. As in trichomycosis, the surrounding skin is not involved. Because of the nodules the hair feels gritty when pulled between the fingers. The nodules of the black variety are composed of a compact mass of wide, closely septate, thick-walled filaments, among which are scattered asci containing eight fusiform ascospores. The nodules of the white variety are composed of wide, closely septate filaments that break up into rectangular elements, budding cells and cocci. Microscopically these nodules are quite different from those seen in trichomycosis. Treatment consisting of vigorous shampoos or shaving, followed by the application of a 1:2000 solution of mercury bichloride or a 3 per cent ammoniated mercury ointment is usually effective.

Otomycosis

Otomycosis is a troublesome disease of the ear canal from which a wide variety of fungi have repeatedly been isolated. The majority of these fungi are saprophytic species, and their role in the disease is not completely understood. The infection is characterized by an exudative inflammation of the ear canal, which may extend to the external ear. Epithelial débris forms somewhat large masses that may interfere with hearing. An extensive pruritus, more noticeable at night, usually accompanies the infection. Treatment is directed toward the removal of all débris and keeping the ear canal dry.[9–12] Drugs having a bactericidal action should be used as a paint; these include a 1 per cent aqueous solution of gentian violet, a 1 per cent aqueous solution of silver nitrate and a 1 per cent aqueous solution of brilliant green. The sulfonamides, especially sulfanilamide, used as a dusting powder have also been found extremely useful. It can be seen that the use of these drugs is aimed at a possible primary bacterial infection of the ear canal as the underlying cause of the disease. Careful observation must be maintained, because of the danger of sensitization to the sulfonamides.

Dermatomycoses

Fungus infections belonging to the category of dermatomycoses are also superficial diseases of the hair, skin or nails, but they are caused by a related group of fungi, the dermatophytes. This group includes the genera Trichophyton, with about twelve species, Microsporum, with three species, and Epidermophyton, with a single species.

Microscopical examination of the infected hair, skin or nails in a 10 to 40 per cent potassium hydroxide preparation is the best method of ensuring an accurate diagnosis of this type of infection. Several modifications of this technic are advocated for preserving specimens for teaching purposes.[13–15]

Wood's light (filtered ultraviolet light), which causes infected hairs to fluoresce, is a great aid in the diagnosis and management of ringworm infection of the scalp.[16] Hairs that fluoresce under this light should be examined microscopically for the presence of fungi. Since successful treatment de-

pends on complete epilation of the infected hairs, the Wood's light serves as an important aid in discovery and ultimate eradication of these foci of infection.

Such preparations as are described above confirm the clinical diagnosis of fungus infection, but they cannot be used for the identification of the invading fungus. Trichophyton, Microsporum and Epidermophyton are similar in appearance when seen in potassium hydroxide preparations of infected skin or nails. Infected hair, however, usually reveals a definite mode of invasion by the genera Trichophyton and Microsporum. Since growth outside or within the hair shaft, or both, serves only as a generic character, it is necessary to culture the infected material to determine the species. It can be therefore seen that a complete identification of the invading fungus in all cases, whether the hair, skin or nails are affected, is possible only by obtaining cultures.

Such cultures are best secured by inoculating Sabouraud's glucose agar slants with several pieces of the infected material. When growth becomes established — in two to three weeks — preparations of the cultures in lactophenol cotton blue for microscopic examination reveal structures that allow their identification. The most useful structures for this purpose are the spore types and accessory organs.[16–18]

The genus Microsporum is characterized by numerous large, fusiform (spindle-shaped) macroconidia (fuseaux) and relatively few small, single-celled microconidia (aleuriospores). Whereas the species *M. canis* and *M. gypseum* produce macroconidia in abundance, *M. audouini* produces abortive types of macroconidia or none at all. In culturing these species on rice medium these differences become apparent.[19]

The genus Trichophyton is characterized by a scarcity of clavate (club-shaped) macroconidia and numerous small, single-celled microconidia produced in grapelike clusters or singly along the hyphae. The macroscopic appearance of the cultures also serves to identify the species Trichophyton. The type of growth — powdery, cottony, smooth or waxy — the configuration and the pigmentation allow these fungi to be identified as *T. rubrum*, *T. rosaceum*, *T. gypseum*, *T. crateriform* or *T. faviform*. These species are not numerous, but can usually be identified only by those familiar with them.

Identification of the single species of the genus Epidermophyton, *E. floccosum*, presents no difficulty. The fungus grows on Sabouraud's medium as a powdery, sulfur-colored fungus and produces clusters or groups of short, stubby, few-celled, club-shaped macroconidia. No microconidia are produced by this fungus in culture. As the growth becomes older the culture reveals numerous chlamydospores.

The dermatomycoses show a wide variety of clinical types, depending somewhat on the location of the infection on the body and the type of fungus causing the infection. It is not possible, however, constantly to associate the same fungus with a particular type of lesion, that is, favus may be caused by *T.* (*Achorion*) *schoenleini*, *T.* (*Achorion*) *violaceum*[20] or *M.* (*Achorion*) *gypseum*.[21] Whereas distinct clinical types of infection are recognized, the etiologic agent can be identified only by culture.

Tinea Pedis

This infection is known as "athlete's foot," dermatophytosis, epidermophytosis and so forth, but is probably better designated as tinea pedis. It is the most frequent of all the fungus infections, and the one causing the greatest concern among the armed forces. A simplification of the clinical types of this infection includes the acute, subacute and chronic forms caused by species of Trichophyton and by *Epidermophyton floccosum*.

The acute infection is characterized by vesicular or vesiculopustular eczematoid lesions, which usually begin between the toes but spread rapidly over the feet or along the soles. The vesicles contain a clear serous fluid until secondary pyogenic infection has taken place. This secondary infection produces ulcerating lesions, which spread rapidly. The foot becomes edematous and painful, with a rapidly developing cellulitis, lymphangitis or lymphadenitis. During this phase systemic reactions may occur.

Vigorous treatment of the acute infection must be avoided until the symptoms have disappeared. Compresses of a saturated solution of boric acid, a 1:4000 solution of potassium permanganate or physiologic saline solution should be used constantly, with the patient in bed and the feet elevated. If the secondary pyogenic infection is caused by a staphylococcus or streptococcus, penicillin should be used. After the acuteness of the lesions has subsided, half-strength Whitfield's ointment or 10 per cent sodium propionate in a water-soluble base may be employed. Treatment should be continued for a week or two after the lesions have healed. A dusting powder should be used as a prophylactic.

The subacute infection is characterized by vesicles or vesicopustules of a spreading type, usually starting between the toes. Absence of a superimposed secondary pyogenic infection of the vesicles permits this type of infection to be managed more easily than otherwise. A lymphangitis or lymphadenitis may result, however, and conservative treatment by compressing should precede the use of keratolytics or fungicidal agents. The same kind of treatment as used in the acute infection is often necessary.

The chronic infection is characterized by fissuring between the toes and an accumulation of soggy dead tissue. Hyperhidrosis is usually present, and treatment must be directed toward controlling this condition. Ointments containing a keratolytic (half-strength Whitfield's ointment) can be used to re-

move the dead and infected tissue. Care should be taken to avoid irritating the skin, which may result in an acute flareup. Dusting powders employed as a prophylactic and also as a drying agent are beneficial.

That there is no specific method of treating cases of tinea pedis has been clearly demonstrated by the recent appeals of the medical services of the Army and Navy for help in combating this type of infection. This fact has brought about in vitro studies of new drugs that might prove to be more effective fungicidal or fungistatic agents.[22–24] Concise outlines of management have also been published, as well as data concerning the clinical trial of new drugs. Peck and Schwartz[25] have outlined a plan of treatment and have given numerous prescriptions that prove helpful in various types of infection. Crittenden and Joiner[26] have used cotton hose impregnated with copper sulfate or copper acetate. Bograd[27] has used ethyl chloride as a spray to cover infected areas; Wallace et al.[28] have used a chlorophyl ointment. Recently Keeney and Broyles[29] have reported on the use of propionate acid and the higher fatty acids as beneficial therapeutic and prophylactic agents. No standard method of treatment has, however, resulted from these studies.

Recurrence of infection may result from a previous inadequate treatment of the infected foci or from reinoculation through contaminated contacts. Prevention must therefore include a thorough search for remaining foci of infection and adequate instructions to the patient concerning how contacts may best be avoided.

Shoes, socks, stockings and clothing may be sterilized by formaldehyde vapor. The articles should be placed in a container with a tight-fitting cover, along with old rags or crumpled newspapers soaked with the formaldehyde. The fumes should kill all fungus material in a period of twenty-four hours. These articles are then well aired to avoid a subsequent dermatitis. Cotton socks may be boiled for twenty minutes or soaked in a 1 per cent solution of liquor cresolis saponatus *U. S. P.* overnight and washed in cold water. Women's stockings may be soaked in 90 per cent grain alcohol for twenty-four hours.

A dusting powder (2 per cent salicylic acid, 3 per cent zinc stearate, 6 per cent boric acid, 10 per cent starch and 79 per cent powdered talc) should be used in the shoes and socks and dusted on the feet. Also, the feet may be painted once or twice a week with a sodium propionate lotion, containing 8.2 per cent sodium propionate, 1.2 per cent propionic acid and 10 per cent N-propyl alcohol. The feet should be kept clean, clean socks should be worn every day, and if excessive perspiration is serious, a drying agent (aluminum acetate) should be occasionally used.

The patient should be warned about possible places of contamination, that is, shower baths or bathroom floors. Newspapers or similar material that is easily disposed of should be used on the bathroom floor instead of mats. The tub should be thoroughly cleaned and dried after use. A rubber mat for the shower floor should be washed and placed in the sun to dry. Slip-on rubber sandals can be worn in the showers, and to and from them in gymnasiums and swimming pools. Too much reliance should not be placed on the foot baths to be found in these places. Often they are hurriedly used, become diluted or contaminated with organic materials and are not frequently freshened. All these factors, together with the doubtful fungicidal activity of the various types of foot baths advocated, destroy the value of this type of prophylactic measure.

Tinea Corporis

Fungus infections of the glabrous skin, which have been designated as tinea glabrosa, tinea circinata, ringworm of the smooth skin and so forth, are caused by species of Microsporum and Trichophyton. The lesions resulting from this type of infection vary greatly, and the clinical diagnosis should be confirmed by laboratory examinations of material obtained from the lesions and by culture.

Infections on the glabrous skin vary from extremely superficial scaly annular lesions to an erythematous squamous or deep granulomatous type. The usual lesion begins as a red papule, which spreads peripherally while healing in the center. The erythematous border has many minute vesicles and pustules, with some crusting. This type of circular lesion with reddened active border and healing scaly center is typical of ringworm, or tinea circinata, of the skin.

If the lesion begins as a vesicle or group of vesicles that break down and form a rather large crusted area with peripheral vesiculation but no central healing, the lesion is usually referred to as the eczematous type. Such lesions may be single or multiple, coalescing to form large configurations.

Suppurative, deep, granulomatous lesions begin as red, indurated nodules centered around perifollicular abscesses. Discharge of pus and ulceration of the skin are indications of a severe infection.

The type of infecting organism cannot always be determined by the clinical appearance of the lesions. It is now well known that a single fungus can produce different types of lesions and that different fungi can produce similar lesions. In some cases, however, certain species are somewhat consistent in the type of lesion that they produce. The configuration of the lesions found in tinea imbricata of the tropics and of South and Central America is characteristic of an infection produced by *T. concentricum*. Also, the cuplike structures (scutula) on the scalp and glabrous skin in tinea favosa are somewhat characteristic of invasion by *T.* (*Achorion*) *schoenleinii*. It must be remembered, however, that

both *M.* (*Achorion*) *gypseum*[21] and *T.* (*Achorion*) *violaceum*[20] have also been isolated from typical favus lesions. It has been pointed out that *T. rubrum* (*purpureum*) also produces a somewhat specific reaction.[30]

The only reliable means of determining the type of invading fungus is culture and identification of the resulting growth. Material for culture is obtained from the erythematous border of the lesions by scraping or by curetting the tops of vesicles. This material should be examined microscopically in potassium hydroxide and cultured on Sabouraud's glucose agar slants. Since an accurate prognosis depends on the type of infecting organism — that is, *T. rubrum* and *T. schoenleinii* produce stubborn, resistant infections, — cultures should be obtained and identified whenever possible.

Treatment of tinea corporis is not difficult unless the invading fungus happens to be either of the two mentioned above. Even in these cases, successful treatment is possible, but it must be prolonged and more intensive.

Ointments (5 per cent ammoniated mercury, 3 per cent salicylic acid and 5 per cent ammoniated mercury or 3 per cent precipitate sulfur and 3 per cent salicylic acid) or a 3.5 per cent tincture of iodine should be applied twice daily. When the vesicular lesions become crusted, it is necessary to remove the crusts and thoroughly rub in the ointment. Cure should be effective in two weeks.

Lesions on the glabrous skin that simulate in every detail the clinical appearance of active fungus infections occasionally fail to heal after appropriate treatment. Serious consideration should be given to such cases to establish whether fungi are locally present in the lesions or whether the lesions are the result of hypersensitivity, that is, dermatophytids or secondary eruptions occurring in a sensitized person. These dermatophytids may occur anywhere, but are found particularly on the palmar aspects of the hands as a result of a hematogenous spread of a fungus or its products from a primary focus of infection elsewhere on the body. These primary foci are usually confined to the feet,[31] are unnoticed by the patient, and sometimes are discovered only after a thorough investigation. Occasionally, too vigorous treatment of tinea pedis causes a generalized dermatophytide reaction. It is therefore necessary to examine microscopically material from lesions of the glabrous skin to establish the presence or absence of fungi. When fungi are not seen in such material, the primary focus of infection must be found and treated. In such cases the dermatophytide reaction subsides as the primary focus heals.

Tinea Cruris

Tinea cruris, or ringworm infection of the groin, also known as tinea inguinale, eczema marginatum, jockey itch, dhobie itch and so forth, is a circumscribed, well demarcated infection of the crural region usually caused by *Epidermophyton floccosum* and occasionally by species of Trichophyton.

This infection was known to Harz[32] in 1871, at which time he cultured *E. floccosum* from it. The lesions are usually bilateral, elevated, papular, scaly, red areas with a sharply demarcated border of vesicopustules. Although the inner thighs are the areas usually involved, the infection may spread to the sacrum or involve the pubic areas. The disease is more frequent in males than in females but is often seen in the latter. Epidemics have been reported[33] in regions where people were living closely together under crowded conditions.

Treatment with ointments (half-strength Whitfield's ointment and 3 per cent precipitated sulfur and 3 per cent salicylic acid in petrolatum) or with Castellani's paint is usually effective in two weeks. Occasional stubborn cases necessitate prolonged treatment. Careful laundering of wearing apparel is important to avoid reinfection.

Tinea Unguium

Ringworm of the nails or onychomycosis of the hands or feet usually accompanies tinea pedis or infection elsewhere on the body, but can occur as the only presenting lesion. This disease is caused by species of Trichophyton, *Epidermophyton floccosum* and *Candida* (*Monilia*) *albicans*.

Nails infected by the dermatophytes show yellowish discoloration, and become lusterless, friable and thickened, often with great amounts of material beneath the nail. Paronychia is not an accompanying symptom. Material should be scraped from the discolored or friable areas and from beneath the nail for microscopic examination and culture. The fungi appear as branching filaments when the infection is caused by the skin fungi.

Nails infected with *C. albicans* have an accompanying paronychia. The nails become thickened, grooved and brownish but remain translucent and do not become brittle. This fungus appears as small, budding, egg-shaped cells in the infected material.

Treatment of nails infected with dermatophytes consists of filing or scraping the infected portions of the nail as thoroughly as possible. The scraped nail may be painted with chrysarobin (20 per cent in chloroform), taking care to avoid contact with the skin, rubbed with sulfur salicyclic acid ointment (10 per cent each of precipitated sulfur and salicylic acid in equal parts of lanolin and rose water ointment) or painted with 1 per cent iodine in alcohol. Before each medication the old material should be scraped off the nail. Surgical evulsion of a nail is sometimes necessary. Nails infected with *C. albicans* should also be scraped and the nails soaked in a 1:4000 aqueous solution of potassium permanganate three times daily, followed by a paint containing 1 per cent gentian violet or an ointment

containing 5 per cent ammoniated mercury. Whether infection is caused by the dermatophytes or by *C. albicans*, the treatment is prolonged and may last for months before a cure can be expected.

Tinea Barbae

Ringworm of the beard, known as sycosis parasitica, tinea sycosis and so forth, is a stubborn, chronic fungus infection of the bearded region of the face and neck, with rare involvement of the upper lip, caused by species of Trichophyton and Microsporum.

Two types of infection may be encountered in the bearded area: a superficial dry lesion with a central scaly area and an active vesiculopustular periphery or areas of perifollicular pustules with lusterless hairs progressing to red, deep-seated nodules and boggy masses with adenitis of the regional lymph nodes. Such areas are undermined, and extrusion of purulent material occurs, with resulting crust formation. The hairs are brittle and easily epilated. Involvement of the upper lip has been reported,[34, 35] but is rare. Microscopical examination of material from the lesions is the only means of determining the fungus nature of the infection.

The patient should be instructed in the sterilization of his shaving articles. Manual epilation of all infected hairs is necessary for complete cure. In some cases x-ray epilation may be necessary. Compresses of hot boric acid solution, a 1:4000 aqueous solution of potassium permanganate or Vleminckx's solution, diluted 1:10, followed by a 5 per cent ammoniated mercury ointment rubbed well into the skin, should prove successful.

Tinea Capitis

Ringworm infection of the scalp, tinea capitis, is essentially a disease of childhood, with a variety of clinical appearances, and is caused by species of Trichophyton and Microsporum.

The appearance of lesions on the scalp caused by the dermatophytes varies according to the type of infecting fungus and the response of the patient. Some species of Microsporum and Trichophyton cause an inflammatory reaction leading to large, boggy, tumorlike masses (kerion). In such areas, the infected hairs are dislodged easily and there is a tendency to spontaneous cure. Other species do not evoke an inflammatory reaction and are more difficult to manage and treat.

Infection by species of Microsporum usually results in a few scaly, gray patches in which the hairs are broken off 3 to 4 mm. from the surface of the scalp. Microscopically, the hairs are seen to be surrounded by a sheath of angular spores arranged in a mosaic pattern.

Infection by species of Trichophyton results in a variety of lesions, depending on the particular species involved. Infection by *Trichophyton schoenleinii*, the usual cause of favus, is characterized by the formation about the hair follicle of a yellow crust with a depressed center, giving a cuplike appearance. Such cups, or scutula, contain mycelium and cellular débris and are pierced by the hairs. Microscopically, the hairs are seen to be of the endothrix type, with invasion of the fungus inside the hair shaft. A seborrheic eczema type of lesion with diffuse superficial scaling may also be caused by this fungus. Examination of the hairs is necessary for a differential diagnosis. Infection by other endothrix species (*T. violaceum* and *T. acuminatum*) may be characterized by small, scattered, scaly crusts over the scalp with the hairs broken off at the surface. The follicles protrude and have a black center (black-dot ringworm), or the hairs may not be broken off but be folded in the scales of the crusts forming the lesion (*T. tonsurans*).

Species of Trichophyton belonging to the ectothrix group, such as *T. mentagrophytes* (*gypseum*), in which the fungus is seen outside and surrounding the hair shaft as parallel rows of spores, produce inflammatory and suppurative lesions leading to kerion formation. This type of infection may be mistaken for pyodermia, and the only satisfactory diagnosis is that based on a microscopic examination of the hair. Since an inflammatory reaction may develop a sensitivity of the skin, patients with kerion of the scalp may exhibit rashes on the trunk or extremities. This type of reaction has been known for some time[31, 36] and, as mentioned previously under tinea pedis, is the result of a hematogenous spread of the fungus or its products from a primary focus of infection. Such lesions, dermatophytides, do not contain the fungus, are an allergic manifestation and disappear as the primary focus heals.

Treatment of tinea capitis must be guided by the type of fungus causing the infection. *M. audouini*, *T. schoenleinii*, *T. violaceum* and *T. tonsurans* cause resistant infections that are difficult to manage. The lesions of *M. audouini*, however, tend to heal spontaneously as puberty is reached. *T. schoenleinii* and *T. violaceum* produce lesions that do not heal spontaneously at puberty but remain through the adult years. On the other hand, *M. canis*, *M. gypseum* and *T. mentagrophytes* cause lesions that may heal spontaneously at any time, especially if an inflammatory reaction is induced. It is therefore necessary to obtain cultures and identify the fungus from each case for a proper evaluation of prognosis and treatment.

Treatment is directed toward the removal of all infected hairs. Wood's light is invaluable as an aid in detecting these hairs and should be constantly used during the management of the disease. Hairs infected with the following fungi fluoresce under this light: *M. audouini*, *M. gypseum*, *M. canis*, *T. schoenleinii*, *T. violaceum*, *T. tonsurans* and *T. mentagrophytes*.

A conservative type of treatment may be used when the infection is one that is likely to heal spon-

taneously. An ointment containing 5 per cent ammoniated mercury or 10 per cent sulfur ointment with iodine crystals should be rubbed well into the scalp. Daily shampooing, with a stiff brushing, removes the loosened infected hairs. The shampoo should be followed each time with the ointment.

Treatment of the infection, which is likely to remain until puberty or be carried over into adulthood, demands better methods of epilation. Manual epilation with forceps is practical only when small areas of the scalp are infected, and should be repeated every four days. For larger areas, the hair should be clipped close and adhesive plaster applied tightly and pulled off to remove the loosened hairs. An ointment of 10 per cent ammoniated mercury rubbed into the scalp will prevent infection of healthy areas, and an adhesive-plaster patch over the infected areas will prevent the loosened hairs from falling out to cause reinfection or epidemics. Roentgen-ray epilation may be desirable in certain cases, but should be done only by one fully experienced in its use.[37] Thallium acetate should be used only when contraindications are lacking and the patient is hospitalized.

Estrogenic substances[38] in the treatment of tinea capitis caused by *M. audouini* and trichophyton[39] as a therapeutic agent for ringworm of the scalp have not as yet given satisfactory results.[16]

Subcutaneous Mycoses

Infections of the subcutaneous tissues are caused by a wide variety of fungi, which produce lesions simulating those of syphilis, tuberculosis, and pyogenic infections as well as granulomas and neoplasms. Three of the frequent types of such infections will be discussed below.

Chromoblastomycosis

This disease, often referred to as chromomycosis or verrucous dermatitis, caused by *Hormodendrum pedrosoi*, *H. compactum* and *Phialophora verrucosa* and thought previously to be of rare occurrence in the United States, has gained widespread interest, owing not only to the increased number of cases encountered in this country but also to the atypical forms of the disease that have been reported.

Chromoblastomycosis is a disease, usually of the lower extremities, producing unilateral lesions of warty papillomatous vegetations (verrucous dermatitis). Fibrosis and blocking of the lymphatics produce an elephantiasis; ulceration and secondary infection may occur. There is no systemic involvement or involvement of the bones. and the general health remains good.

Recent reports in the literature,[40–42] however, have referred to the protean nature of the infection and to the difficulty of making a clinical diagnosis before a long-standing infection brings about the typical verrucous appearance of the lesion. Also, the diagnosis may not be readily apparent if lesions occur in areas of the body other than on the feet, such as, the hand,[43–46] the arm,[47–49] the face,[40, 50] the neck[51] and the buttock.[52]

Diagnosis should be made by laboratory examination of pus, crusts or biopsy sections in which the unmistakable dark-brown splitting bodies of the fungus are found. Since the different fungi (*Hormodendrum pedrosoi*, *H. compactum* and *Phialophora verrucosa*) known to produce this disease appear identical in tissue, cultures on Sabouraud's glucose agar should be made to determine exactly the fungus responsible for a given case.

There is no general agreement on the nomenclature for these fungi.[42, 53, 54] The various spore types produced by the single species *H. pedrosoi* in culture have allowed this fungus to be placed in numerous genera according to the emphasis placed on a given spore type.

Treatment of the extensive lesion is unsatisfactory. Potassium iodide, with and without x-ray therapy, and iontophoresis[49] have been used. Early lesions, if diagnosed, should be removed by excision or destroyed by electrocoagulation.

Maduromycosis

This disease, also referred to as Madura foot or mycetoma, is produced by the greatest assortment of heterogeneous fungi. In spite of this, however, it is generally agreed that the disease is a clinical entity, and its pathology remains fairly constant regardless of the type of fungus causing the infection.

Deep-seated chronic infections of the subcutaneous tissues of the feet cause, over long periods of time, swelling and clubbing of the involved member, resulting in marked deformity. This may be accompanied by destruction of the small bones of the foot and extensive fusion of these structures. There are no systemic reactions and little pain, and the foot can be used with slight discomfort.

Scattered over the deformed foot may be seen numerous abscesses, which rupture, drain and develop into fistulas. The serosanguineous fluid from such fistulas contains the macroscopic colored grains (white, black, yellow or red) that are diagnostic when seen microscopically. Such grains are composed of a mass of broad, septate, branching hyphae containing numerous chlamydospores. The width of the hyphae and the presence of chlamydospores differentiate these grains from the granules seen in actinomycosis. In the latter disease, the granules are made up of a mass of delicate hyphae, 1 micron in diameter, which usually terminate in club-shaped swellings at the periphery of the granule.

These differences early led to the classification of mycetoma into two categories by Chalmers and Archibald[55]: actinomycotic mycetoma, caused by species of Actinomyces and maduromycosis, caused by species of higher fungi and molds. Although this classification is adhered to by many investigators,

some retain a single term, maduromycosis, since the disease is clinically and pathologically an entity regardless of the particular fungus found to be associated with a given infection.

Recently, however, Symmers and Sporer[56] have reported an infection of the hand in a native American in which new histologic features were observed. Whether these findings were the result of an infection by the particular fungus responsible for their case and do not occur in infections by other hyphomycetes can be determined only by a comparative study of tissues from many cases. At the present time these authors believe that maduromycosis is a distinct disease quite different clinically, pathologically and mycologically from any other disease, particularly actinomycosis.

The various fungi that have been isolated from mycetoma are listed by Conant et al.[57] Of the 38 cases reported from the United States, only 11 can be classified as maduromycosis as proved by culture. The following fungi have been isolated: *Allescheria boydii*,[58] *Madurella americana*,[59] *M. ikedai*,[60] *M. lackawana*,[61] *Aspergillus nidulans*,[62] *Monosporium apiospermum*[57, 63–66] and *Torula* (?) *jeanselmei*.[56] Emmons[67] has shown that two of these fungi, *Allescheria boydii* and *M. apiospermum*, are but different phases (an ascomycetous and the imperfect stage) of a single organism.

Treatment of maduromycosis caused by the higher fungi is not satisfactory. Secondary infections by pyogenic organisms may be controlled by using sulfonamides or penicillin. The usual case, however, requires amputation.

Sporotrichosis

Whereas other fungus infections involving primarily the subcutaneous tissues are caused by a group of fungi, sporotrichosis is caused by the single organism *Sporotrichum schenckii*. Although this fungus can and does infect the entire body, producing widespread disseminated lesions, the disease is discussed among those involving the subcutaneous tissues because it is this type of infection that is encountered more frequently in the United States.

The initial lesion follows an abrasion of the skin, usually on the fingers or hands, and presents itself as a superficial necrotic ulcer that fails to heal under ordinary treatment. Lymphatics draining the area show a marked inflammation and develop multiple deep nodular subcutaneous abscesses, which usually terminate in ulceration. The intervening lymphatic vessels become thickened and cord-like in consistence. The regional lymph nodes are not involved, and the patient presents few, if any, systemic symptoms.

A clinical diagnosis of sporotrichosis is confirmed by obtaining cultures of *S. schenckii* from the ulcers or unruptured subcutaneous nodules.

This so-called "localized" lymphatic sporotrichosis is the usual type of case encountered in the United States. Moore and Kile,[68] Forbus[69] and Singer[70] have reported some of the rare disseminated cases of the disease. In Europe, however, extensive infections are the rule and any organ of the body may be affected. De Beurmann and Gougerot[71] classify the clinical types as lymphatic, disseminated, epidermal, mucosal, skeletal and visceral.

Sporotrichoses may be acquired from plants or infected animals. Foerster[72, 73] reported cases following injury by barberry thorns and considered the disease to be an occupational hazard among farmers and horticulturists. Meyer[74] has reported infections in man following the bites of horses, dogs, hens and parrots. Anderson and Spector[75] have reported an associated sporotrichosis with rat-bite fever.

Treatment of sporotrichosis is most satisfactory with potassium iodide. Of all the fungus infections, sporotrichosis is the only one that responds specifically to this drug. Occasionally, however, an exceptional case may not respond to iodides.[76, 77] In such cases sulfonamides may be used either orally[78] or locally.[79]

(To be concluded)

References

1. Saffron, M. H. Dermatology and war. *Mil. Surgeon* **91**:559-564, 1942.
2. Downing, J. G. Dermatophytosis and occupational dermatitis. *J. A. M. A.* **125**:196-200, 1944.
3. Goldstein, D. M., and Louie, S. Primary pulmonary coccidioidomycosis: report of epidemic of 75 cases. *War Med.* **4**:299-317, 1943.
4. Marquardt, F. Die Kultur des Mikrosporon furfur. *Dermat. Wchnschr.* **104**:177-180, 1937.
5. Moore, M. Cultivation of *Malassezia furfur*, etiological agent of pityriasis (tinea) versicolor. *Mycopathologia* **1**:53-61, 1938.
6. Castellani, A., and Wilkinson, A. G. Trichomycosis axillaris flava, rubra, and nigra. *Brit. J. Dermat.* **34**:255-266, 1922.
7. Fonseca, O. da Filho, and Area Leao, A. E. de. Sobre as cogumelos da piedra brasilara. *Mem. Inst. Oswaldo Cruz.* Supp. **4**:124, 1938.
8. Mackinnon, J. E., and Schouten, G. B. Investigaciones sobre las enfermedades de los cabellos denominadas "piedra." *Arch. Soc. de biol. de Montevideo* **10**:227-266, 1942.
9. McBurney, R., and Searcy, H. B. Otomycosis: investigation of effective fungicidal agents in treatment. *Ann. Otol., Rhin. & Laryng.* **45**: 988-1008, 1936.
10. Reeh, M. J. Treatment of otomycosis. *Ann. Otol., Rhin. & Laryng.* **51**:146-152, 1942.
11. Whalen, E. J. Fungous infections of external ear. *J. A. M. A.* **111**: 502-504, 1938.
12. Senturia, B. H. Treatment of external otitis. I. Local sulfonamide therapy. *Laryngoscope* **54**:277-286, 1944. Senturia, B. H., and Wolf, F. T. Treatment of external otitis. II. Action of sulfonamide compounds on fungi isolated from cases of otomycosis. *Arch. Otolaryng.* **41**:56-63, 1945.
13. Swartz, J. H., and Conant, N. F. Direct microscopic examination of skin method for determination of presence of fungi. *Arch. Dermat. & Syph.* **33**:291-305, 1936.
14. Berberian, D. A. Method of staining hair and epithelial scales. *Arch. Dermat. & Syph.* **36**:1171-1175, 1937.
15. Bernhardt, E. Simplified method for staining fungi in skin and in nails. *Arch. Dermat. & Syph.* **48**:533-535, 1943.
16. Lewis, G. M., and Hopper, M. E. *An Introduction to Medical Mycology.* Second edition. 342 pp. Chicago: Year Book Publishers, Incorporated, 1943.
17. Emmons, C. W. Dermatophytes; natural grouping based on form of spores and accessory organs. *Arch. Dermat. & Syph.* **30**:337-362, 1934.
18. Conant, N. F., et al. *Manual of Clinical Mycology.* 348 pp. Philadelphia: W. B. Saunders Company, 1944.
19. Conant, N. F. Studies in genus *Microsporum*: cultural studies. *Arch. Dermat. & Syph.* **33**:665-683, 1936.
20. Bloch, B. Das Achorion violaceum, ein bisher unbekannter Favuspilz. *Dermat. Ztschr.* **18**:815-833, 1911.
21. Bodin, E. Sur un nouveau champignon du favus (achorion gypseum). *Ann. de Dermat. et Syph.* **8**:585-602, 1907.
22. Lewis, G. M., and Hopper, M. E. Effect of sulfanilamide and its derivatives on fungi: preliminary in vitro experiments. *Arch. Dermat. & Syph.* **44**:1101-1103, 1941.
23. Diamond, N. S., and Thompson, K. W. Effect of sulfonamide drugs on trichophytons in vitro. *J. Invest. Dermat.* **5**:397-402, 1942.
24. Keeney, E. L., Ajello, L., and Lankford, E. Studies on common pathogenic fungi and on Actinomyces bovis. II. In vitro effect of sulfonamides. *Bull. Johns Hopkins Hosp.* **75**:393-409, 1944. III. In vitro effect of penicillin. *Ibid.* **75**:410-416, 1944.
25. Peck, S. M., and Schwartz, L. Practical plan for treatment of superficial fungus infections. *Pub. Health Rep.* **58**:337-345, 1943.

26. Crittenden, P. J., and Joiner, L. S. Cotton hose as vehicle for fungicide in treatment of athlete's foot. *J. Lab. & Clin. Med.* **29**:606-608, 1944.
27. Bograd, N. Treatment of tinea with ethyl chloride. *Arch. Dermat. & Syph.* **48**:511, 1943.
28. Wallace, G. I., Day, J. K., and Moorman, H. E. Chlorophyl ointment in treatment of dermatophytosis of feet and similar lesions. *Arch. Dermat. & Syph.* **49**:128-131, 1944.
29. Keeney, E. L., and Broyles, E. N. Sodium propionate in treatment of superficial fungous infections. *Bull. Johns Hopkins Hosp.* **73**: 479-487, 1943.
30. Lewis, G. M., Montgomery, R. M., and Hopper, M. E. Cutaneous manifestations of Trichophyton purpureum (Bang). *Arch. Dermat. & Syph.* **37**:823-839, 1938.
31. Williams, C. M. Diagnosis of some eruptions on hands and feet. *Arch. Dermat. & Syph.* **5**:161-172, 1922. Dermatophytid complicating dermatophytosis of glabrous skin. *Ibid.* **13**:661-669, 1926.
32. Harz, C. O. Einige neue Hyphomyceten Berlin's und Wien's nebst Beiträge zur Systematik derselben. *Bull. Soc. Imp. Nat. Moscow* **44**:88-147,1871.
33. Mercer, S. T., and Farber, G. J. Epidemic of ringworm due to Epidermophyton floccosum (inguinale). *Arch. Dermat. & Syph.* **32**: 62-68, 1935.
34. Davidson, A. M., and Dowding, E. S. Tinea barbae of upper lip. *Arch. Dermat. & Syph.* **26**:660-662, 1932.
35. Lawless, T. K. Tinea sycosis of upper lip. *Arch. Dermat. & Syph.* **34**: 118-121, 1936.
36. Bloch, B. Die Trichophytide. In Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*. Vol. 2. Berlin: Julius Springer, 1928. Pp. 564-606.
37. MacKee, G. M. *X-rays and Radium in Treatment of Diseases of Skin*. 830 pp. Philadelphia: Lea & Febiger, 1938.
38. Poth, D. O., and Kaliski, S. R. Estrogen therapy of tinea capitis; preliminary report. *Arch. Dermat. & Syph.* **45**:121-128, 1942.
39. Lewis, G. M., and Hopper, M. E. Ringworm of scalp: comparative reactions to cutaneous tests with trichophytin in children with and without ringworm of scalp: evaluation of therapy with stock vaccines in types of infection resistant to treatment. *Arch. Dermat. & Syph.* **36**:821-832, 1937.
40. Moore, M., and Mapother, P. Chromomycosis of face: report of case and study of causative organism, Phialophora verrucosa. *Arch. Dermat. & Syph.* **41**:42-54, 1940.
41. Weidman, F. D., and Rosenthal, L. H. Chromoblastomycosis: new and important blastomycosis in North America: report of case in Philadelphia. *Arch. Dermat. & Syph.* **43**:62-84, 1941.
42. Binford, C. H., Hess, G., and Emmons, C. W. Chromoblastomycosis: report of case from continental United States and discussion of classification of causative fungus. *Arch. Dermat. & Syph.* **49**:398-402, 1944.
43. MacKinnon, J. E. Estudio del primer caso uruguayo de cromoblastomicosis y "revista critica" sobre la enfermedad. *Arch. urug. de med., cir. y especialid.* **5**:201-226, 1934.
44. Takahashi, Y. Zur Chromoblastomykose: über Chromoblastomykose hervorgerufen durch Hormodendron japonicum n. sp. *Jap. J. Dermat. & Urol.* **41**:53-62, 1937.
45. Gomes, J. M. Chromoblastomycosis caused by fungus of genus Hormodendron. *Arch. Dermat. & Syph.* **38**:12-18, 1938.
46. Emmons, C. W., Hailey, Howard, and Hailey, Hugh. Chromoblastomycosis: report of sixth case from continental United States. *J. A. M. A.* **116**:25-28, 1941.
47. da Fonseca, O., Jr., and de Arêa Leão, A. E. As chromoblastomycoses. *Rev. med.-cir. do Brasil* **38**:197-216, 1930.
48. Carrión, A. L. Chromoblastomycosis: new clinical type caused by *Hormodendrum compactum*. *Puerto Rico J. Pub. Health & Trop. Med.* **11**:663-682, 1936.
49. Martin, D. S., Baker, R. D., and Conant, N. F. Case of verrucous dermatitis caused by *Hormodendrum pedrosoi* (chromoblastomycosis) in North Carolina. *Am. J. Trop. Med.* **16**:593-619, 1936.
50. Kano, K. Über die Chromoblastomykose durch einen noch nicht als pathogen beschriebenen Pilz: Hormiscium dermatitidis n. sp. *Arch. f. Dermat. u. Syph.* **176**:282-294, 1937.
51. Pedroso, A., and Gomes, J. M. Sobre quatro casos de dermatite verrucosa produzida pela *Phialophora verrucosa*. *Ann. paulist. de med. e cir.* **11**:53-61, 1920.
52. Lane, C. G. Cutaneous lesion caused by new fungus (Phialophora verrucosa). *J. Cutan. Dis.* **33**:840-846, 1915.
53. Moore, M., and de Almeida, F. P. New organisms of chromomycosis. *Ann. Miss. Bot. Gard.* **23**:543-552, 1936.
54. Carrión, A. L. Chromoblastomycosis. *Mycologia* **34**:424-441, 1942.
55. Chalmers, A. J., and Archibald, R. G. Sudanese maduromycosis. *Ann. Trop. M. & Parasitol.* **10**:169-222, 1916.
56. Symmers, D., and Sporer, A. Maduromycosis of hand, with special reference to heretofore undescribed foreign body granulomas formed around disintegrated chlamydospores. *Pathology* **37**:309-318, 1944.
57. Conant, N. F., et al. *Manual of Clinical Mycology*. 348 pp. Philadelphia: W. B. Saunders Company, 1944.
58. Boyd, M. F., and Crutchfield, E. D. Contribution to study of mycetoma in North America. *Am. J. Trop. Med.* **1**:215-289, 1921.
59. Gammel, J. A., Miskdjian, H., and Thatcher, H. S. Madura foot (mycetoma) black grain variety in native America. *Arch. Dermat. & Syph.* **13**:66-77, 1926.
60. Gammel, J. A. Etiology of maduromycosis, with mycologic report on two new species observed in United States. *Arch. Dermat. & Syph.* **15**:241-284, 1927.
61. Hanan, E. B., and Zurett, S. New species of Madurella: isolation and identification in cases of maduromycosis. *Arch. Dermat. & Syph.* **37**:947-966, 1938.
62. Puestow, K. L. Maduromycosis: contribution to study of maduromycosis, with report of case of infection with aspergillus nidulans. *Arch. Dermat. & Syph.* **20**:642-664, 1929.
63. Gay, D. M., and Bigelow, J. B. Madura foot due to *Monosporium apiospermum* in native American. *Am. J. Path.* **6**:325-335, 1930.
64. Jones, J. W., and Alden, H. S. Madurmycotic mycetoma (Madura foot). *J. A. M. A.* **96**:256-260, 1931.
65. Gellman, M., and Gammel, J. A. Madura foot: third case of monosporosis in native American. *Arch. Surg.* **26**:295-307, 1933.
66. Fienberg, R. Madura foot in native American: case of monosporosis. *Am. J. Clin. Path.* **14**:239-246, 1944.
67. Emmons, C. W. *Allescheria Boydii* and *Monosporium apiospermum*. *Mycologia* **36**:188, 1944.
68. Moore, M., and Kile, R. L. Generalized, subcutaneous, gummatous, ulcerating sporotrichosis: report of case with study of etiologic agent. *Arch. Dermat. & Syph.* **31**:672-685, 1935.
69. Forbus, W. D. Pulmonary sporotrichosis. *Am. Rev. Tubrc.* **16**: 599-627, 1927.
70. Singer, J. J. Pulmonary sporotrichosis: report of two cases. *Am. Rev. Tubrc.* **18**:438-443, 1928.
71. De Beurmann, L., and Gougerot, H. *Les Sporotrichoses*. 852 pp. Paris: Feliz Alcan, 1912.
72. Foerster, H. R. Sporotrichosis. *Am. J. M. Sc.* **167**:54-76, 1924.
73. *Idem*. Sporotrichosis, an occupational dermatosis. *J. A. M. A.* **87**: 1605-1609, 1926.
74. Meyer, K. F. Relation of animal to human sporotrichosis. *J. A. M. A.* **65**:579-585, 1915.
75. Anderson, N. P., and Spector, B. K. Rat-bite fever associated with Sporothrix. *J. Infect. Dis.* **50**:344-349, 1932.
76. King, H. Sporotrichosis with report of unusual case. *South M. J.* **20**: 543-546, 1927.
77. Ray, L. F., and Rockwood, E. M. Sporotrichosis: report of case in which it was resistant to treatment. *Arch. Dermat. & Syph.* **46**: 211-217, 1942.
78. Navarro-Martin, A. Sporotrichosis: sulfonamide therapy, with report of case. *Actas dermo-sif.* **32**:271, 1940.
79. Noojin, R. O., and Callaway, J. L. Effectiveness in vitro of sulfonamide compounds on Sporotrichum schenckii: report of five cases of sporotrichosis in North Carolina. *Arch. Dermat. & Syph.* **49**: 305-308, 1944.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 31311

PRESENTATION OF CASE

A thirteen-week-old male infant was admitted to the hospital because of vomiting of blood-streaked material.

The child was the first of twins born seven weeks prematurely. This was the fifth pregnancy of the mother, and labor was short and easy. The birth weight was 3 pounds, 1 ounce. The other twin weighed 2 pounds. Both children vomited frequently, and the other child died after one week. The patient was fed human milk by gavage many times while in the hospital. In eight weeks the child was discharged, weighing 5 pounds. On the day he arrived home he vomited white curds with some dark-brown streaks. During the ensuing five weeks he vomited after almost every feeding, with frequent dark-brown streaks and material among the curds. Three days before admission, just before his evening feeding, the baby vomited a large quantity of dark-brown shiny material. He vomited again after the feeding, and the vomitus was streaked with a dark-brown substance. On the day before admission the baby was taken to a physician. While in the doctor's office the baby vomited. The vomitus, which appeared like that of the past few days, was tested by the physician and found to contain blood. On the evening before admission the baby again vomited large amounts of dark-brown material mixed with curds. While at home, he had been on a formula consisting of 16 ounces of milk and 3 tablespoonfuls of Karo, with no fruit juice or vitamin supplement. During these five weeks he had gained only 7 ounces. The mother stated that she was always careful to "bubble" the child, but despite this he would vomit about ten minutes after each feeding. The mother states that he did not vomit the entire meal. He usually had five bowel movements a day, the stools varying from yellowish and formed to greenish and liquid.

Physical examination revealed a severely undernourished and underdeveloped infant, measuring 47.5 cm. and weighing 5 pounds, 8 ounces. He appeared vigorous, with a lusty cry, and seemed in no distress and fairly well hydrated. There were no skin lesions. The fontanelles were open and flat. Examination of the heart and lungs was normal. The abdomen was normal. No peristaltic waves were seen with feeding, and no masses were felt.

The temperature was normal, the pulse 110, and the respirations 40.

Examination of the blood showed a red-cell count of 3,800,000 with 8.6 gm. of hemoglobin, and a white-cell count of 16,300, with 66 neutrophils, 23 lymphocytes, 9 monocytes and 2 eosinophils. The urine was negative. The bleeding time was 6 minutes, and the clotting time 4 minutes; clot retraction was good. A tourniquet test was negative. The prothrombin time was 20 seconds (normal, 18 to 20 seconds). Vomitus and stool examinations were strongly positive for blood. A Hinton test was negative. A skin tuberculin test in a dilution of 1:100 was negative. The blood was Rh negative. The serum protein was 5.1 gm. per 100 cc. The nonprotein nitrogen, chloride, sodium and phosphorus were normal. The alkaline phosphatase was 13.7 units per 100 cc. A cephalin flocculation test was negative.

X-ray examination of the chest showed an area of increased density, apparently collapse, in the right upper lung field. There was extensive increased density in the left upper and right lower lung fields. Films of the long bones of the forearm showed no definite abnormality. A barium swallow showed the esophagus to be rather wide, but there was no demonstrable fistula between it and the trachea and no constant defects were seen. The stomach was likewise dilated, and in the distal portion there appeared a rather constant filling defect in the region of the lesser curvature. In the proximal portion of the second part of the duodenum there was a rather constant narrowing. During the examination, the barium and food content of the stomach frequently regurgitated into the esophagus. A twenty-four-hour film showed that practically all barium had passed through the duodenum.

Because of the lesion in the lungs the child was started on penicillin, 6000 units every three hours. An exploratory laparotomy was done about two weeks after admission. No duodenal obstruction or any other abnormality was found. The child withstood the operation well but continued to vomit his feedings and large amounts of coffee-grounds material. He was then taken off feedings by mouth and maintained parenterally. When feedings by mouth were resumed, he again started to vomit. Attempts to stop the vomiting with sedation and with atropine were unsuccessful. Thickening of the formula was likewise not helpful. The child went downhill in spite of supportive treatment and died two weeks after the operation.

*On leave of absence.

Differential Diagnosis

Dr. Sidney Farber:* The patient was one of twins. The sibling weighing 2 pounds and dying after one week, with a story of vomiting, might have died because of a congenital malformation. Possibly there was infection or hemorrhage. Hemorrhage in general is the most frequent single finding in premature babies who die within ten days after birth. The fact that both babies vomited may have been merely coincidental or possibly both were suffering from the same type of malformation. Gavage feeding of premature babies is frequently a necessity and saves many lives. It may be the cause of ulceration of the esophagus, however, particularly when the feedings are performed by inexperienced people. Such ulceration may form the starting point for infection, which may end in bacteremia.

We might expect that this baby had evidence of scurvy and rickets in addition to other disturbances of calcification of the bones characteristic of premature babies of this size. The baby's length at thirteen weeks of age was several centimeters less than that of a full-term normal baby at birth, and the weight was roughly one third to one half of the normal weight for a full-term baby of the same age.

The findings in the differential count are of interest but give no specific information concerning a definite diagnosis. I am not familiar with the type of tourniquet test performed on premature babies of this size, but apparently there was no unusual bleeding into the skin after this was done. The tuberculin test is usually done in a dilution of 1:1000, which is not sufficient to exclude tuberculosis. Someone must have thought of that diagnosis, perhaps a tuberculous ulcer of the stomach, and a test in a dilution of 1:100 was carried out before this lead was abandoned. Determination of the Rh factor is part of every routine study of the blood. I am not familiar with any disease associated with Rh blood incompatibility that would manifest itself at the age of eight to thirteen weeks, with bleeding for so many weeks thereafter. The serum protein was below normal but within the range of premature babies of this size. Occasionally with bleeding in the gastrointestinal tract the nonprotein nitrogen is increased, but here it was within normal range.

I am not familiar with the value of information derived from a cephalin flocculation test in a premature baby of this age. Let us take it as it is stated—negative. I do not believe that excludes liver disease.

From the x-ray examination we may exclude obvious rickets, scurvy and any of the important abnormalities of the skeleton associated with prematurity. The report states that the esophagus was wide; it does not say "dilated." It certainly appears to be wider than normal on these films. I assume that the fistula which was looked for was one that might have been acquired secondary to the aspiration of a foreign body, a pin or something of that kind; a congenital tracheoesophageal fistula would not be thought of at this age. May we hear from the roentgenologist?

Dr. Milford D. Schulz: The esophagus is wide, and there are numerous defects within it, which appear to be gas bubbles. I do not see the defect along the lesser curvature of the stomach, mentioned in the protocol. The fluoroscopist must have seen it, unless it is this area on the spot films. Again the constant narrowing of the duodenum apparently was a fluoroscopic observation.

Dr. Farber: You see no evidence of duplication of the esophagus or any mass pressing against it?

Dr. Schulz: No; nor of barium in the lungs. The films of the chest are essentially as mentioned in the protocol, and I do not believe that I can add anything.

Dr. Farber: I am afraid that I can say nothing more concerning the films. We have to rely on the evidence from fluoroscopy that there was a true filling defect in the lesser curvature and duodenum since these findings are not present on the films. The consolidation in the right upper lung field, with a story of vomiting, is perhaps best explained by aspiration of vomitus, which often occurs in a premature baby; but before seeing the x-ray films I suspected that a mass attached to the esophagus compressing the lung might have been present.

It must have been decided at the time of exploration that the story was not simply that of vomiting or blood streaking associated with any of the ordinary diseases of the hematopoietic system. There must have been a suspicion that an organic lesion would be found.

We have a problem here, then, which is unusual — that of vomiting of five weeks' duration before admission and of four weeks' duration after admission, with blood streaking of the vomitus in a small prematurely born infant who had gained little weight since birth. There are several possibilities that should be considered before a definite diagnosis is attempted.

Foreign body, to take the least likely possibility, is fairly frequent in children between one and two years but is relatively rare in small babies of this size, unless some extraordinary accident occurs, such as the swallowing of a safety pin or something of that kind. Foreign bodies may cause definite ulceration, particularly if they are sharp. I recall a child who swallowed a piece of artificial denture immersed in nitric acid and developed a duodenal ulcer, which was cured surgically.

Next in line of possibility are a combination of defects associated with the pancreas and an ulcer of the duodenal surface. An annular pancreas causing constriction of the duodenum can give a picture

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like that described, but it would not account for the filling defect in the lesser curvature. We would have to assume that there was an ulcer of the mucosa of the duodenum or stomach, or both, if we were to give one diagnosis. There are occasional cases of annular pancreas associated with malformation of the portal region, so that portal obstruction is caused and a Banti type of obstruction is produced, with esophageal varices or varices in the stomach. This combination of circumstances is a possible explanation. These diagnoses are unlikely.

Another remote possibility, which we have encountered, is a congenital Eck's fistula associated with portal obstruction and, again, esophageal varices to account for the bleeding. Adhesions associated with malformation of the portal system might have caused the duodenal obstruction. But we are left without an explanation for the defect in the stomach.

More probable are two explanations. The first is that he had duplication of the intestinal tract, probably in several locations. This may occur in one area, or there may be six or seven along the course of the intestinal tract. There is no evidence of duplication of the esophagus; nor evidence in these films of duplication of the stomach compressing the lesser curvature or the duodenum. The x-ray studies would have disclosed such duplication, had it been there. Without evidence, however, I can do no more than mention it. Duplication of the intestinal tract may cause constriction, and there may be hemorrhage over a long period of time because of interference to the blood supply of the duodenum or stomach by the duplication, which receives its blood supply from the same source as the adjacent bowel.

The second probable explanation, and perhaps the most logical one, would account for the bleeding, either a tumor or ulcer in the stomach or duodenum. Tumors of the gastrointestinal tract in infants and children are extraordinarily rare. It might be of interest to mention that Dr. J. Hawkins[1] has found that tumors of the brain in children as compared with those in adults occur in a ratio of 1:8, tumors of the kidney and adrenal gland in a ratio of 1:14, and carcinoma of the stomach and duodenum in a ratio of 1:10,000. Thus, tumors of the stomach and duodenum are rare. The only tumor that I should like to mention is a hemangioendothelioma or hemangioma, which may infiltrate the wall of the stomach or duodenum and may be found in the lower portion of the esophagus. These can bleed regularly and can be responsible for this kind of blood-streaked vomitus.

Our problem here is to find a lesion that caused irritability of the stomach, because the stomach expelled food a few minutes after eating and also caused actual bleeding. The final possibility, therefore, is duodenal ulcer or a combination of duodenal and gastric ulcers. These are more frequent in infancy and childhood than is generally recognized. They may occur in the first or second part of the duodenum or in the pyloric end of the stomach. We have to choose a lesion that not only caused vomiting and bleeding but could not be found at operation. The lesion likeliest to hide itself in a patient of this age is an ulcer or, probably in this case if we take the defect in the lesser curvature of the stomach seriously, two ulcers. Ulcers in young infants of this age are sometimes multiple. If these ulcers are small and are located in the first portion of the duodenum, on the posterior wall or on the medial surface, — the so-called "silent" area of the duodenum, — they may not be readily found at exploration and may be found only with some difficulty at autopsy, when the entire specimen is removed and careful dissection is made posteriorly. Such ulcers usually do not cause bleeding for so long a period of time as we have heard about here. This represents an unusual history for ulcer of the duodenum or of the stomach. In infants or children the story of bleeding is usually a very direct one and death occurs in most cases within twenty-four or forty-eight hours after the onset of hematemesis.

Either a hemangioma of the stomach or duodenum or an ulcer could have been present and yet not have been seen at operation. Therefore in order of probability my diagnoses are question of duodenal or gastric ulcer and question of hemangioma of the duodenum or stomach, perhaps with infiltration of the esophagus. All other possibilities that I mentioned would have to be considered and could not be excluded, nor could their presence be included in any way by the evidence that we have. So far as the lungs are concerned, probably the child had an aspiration pneumonia, the aspirated vomitus and blood first causing atelectasis and then an aspiration pneumonia, with finally a bacterial pneumonia probably superimposed on that.

DR. ALLAN M. BUTLER: One thing in the story intrigues me, namely, the nature of the vomitus. The baby was vomiting blood-streaked material and coffee-grounds material with curds. Was there any bile in the vomitus? This might help in determining whether the difficulty was above or below the stomach. The only important feature of the x-ray films is the esophagus, and I should like to ask Dr. Schulz just how impressive the widening is.

DR. SCHULZ: The esophagus is somewhat wider than it usually is in youngsters of that age, but I do not know how wide it is in an infant who is vomiting as repeatedly as this child was. There is no gas in the small bowel beyond the duodenum, and none in the colon.

DR. BUTLER: The description of the vomitus makes me believe that the lesion was high.

DR. NATHAN TALBOT: In postulating an ulcer in the gastrointestinal tract did Dr. Farber assume an associated lesion elsewhere, or would he be surprised to find associated lesions?

DR. FARBER: Ulcers in infancy and childhood are usually not associated with changes in other areas.

Cushing–Rokitansky ulcers, which are frequently found in the fundus and cardiac end of the stomach, are either agonal or extremely acute.

DR. S. E. THEODORE: Was this patient studied for a hiatus hernia?

DR. FARBER: I excluded that in considering the possible diagnosis on the basis of the x-ray findings and surgical exploration. In one or both the evidence should have been found.

CLINICAL DIAGNOSIS

Intestinal obstruction due to congenital malformation.

DR. FARBER'S DIAGNOSES

Duodenal or gastric ulcer?
Hemangioma of duodenum or stomach?
Aspiration pneumonia.

ANATOMICAL DIAGNOSES

Esophageal ulcer, traumatic (gavage tube).
Aspiration pneumonia, with multiple pulmonary abscesses.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy on this child showed an ulceration measuring about 1.5 cm. in length in the lower third of the esophagus about 1 cm. above the cardiac orifice. It had eroded the epithelium, and its base was red and granular. We found no other abnormalities in the entire gastrointestinal tract. Microscopically the base of the ulcer was composed of active granulation tissue with well marked capillary proliferation, which suggested that this had been present for quite a while. The right upper and the left middle lobes of the lung contained numerous abscesses filled with polymorphonuclears, and surrounding these were large numbers of monocytes filled with fat. These were beautifully demonstrated in preparations stained with scharlach R. There were also fairly extensive areas of pneumonia around the abscesses.

I believe that we can relate the entire case to the use of the gavage tube before the patient entered this hospital. We inquired and tried to find out how often the gavage tube was used and how long it had been kept down. We could not get the exact information, but apparently it was used many times and was kept down for varying lengths of time. The pulmonary lesions were almost certainly due to aspiration of the vomitus, which must have been mostly milk. It is also possible that at times some of the food fed by the gavage tube slipped down the larynx. This case then is an example of just what can occur as a result of improper use of the gavage tube in premature infants, as stated by Dr. Farber in his opening remarks.

DR. FARBER: I had intended to mention that a few years ago Rector and Connerly[2] studied the incidence of gastric mucosa in the esophagus, finding it in about 8 per cent of 1000 infants and children. They raised the question of the relation of such mucosa to the formation of ulcers of the esophagus. In this case I do not believe that we have to rely on that explanation.

DR. CASTLEMAN: This ulcer did not have the fibrinoid base characteristic of a peptic ulcer. It was of good size. I believe that it can be wholly explained on the basis of the gavage tube. Have you not seen ulcers of the esophagus as a result of gavage feeding?

DR. FARBER: Yes, but never one with a history of bleeding so long as this. This case is truly unique.

REFERENCES

1. Hawkins, J. Unpublished data.
2. Rector, L. E., and Connerly, M. L. Aberrant mucosa in esophagus in infants and children. *Arch. Path.* **31**:285-294, 1941.

CASE 31312

PRESENTATION OF CASE

A thirty-two-year-old woman was admitted to the hospital complaining of severe headaches accompanied by nausea and vomiting.

Nine months before admission the patient had become pregnant, and at about the same time she had noted malaise, anorexia and attacks of nausea. She also complained of occasional mild headaches. Ten weeks before admission the headaches became severer and more frequent. Two weeks later, nausea and vomiting appeared and persisted. The patient was hospitalized for a week and showed some improvement following the administration of intravenous fluids and plasma. Four weeks before admission she was again hospitalized, and two weeks later underwent a cesarean section, before the spontaneous onset of labor, because of a contracted pelvis. After this operation the vomiting persisted and became progressively severer. The patient had worn glasses several years for astigmatism. During the month before admission, her vision failed rapidly, so that on admission she could not read but could still distinguish faces. During this period the patient occasionally acted strangely and at times was abnormally moody and sleepy. She had had no convulsions or deafness, but the right side of her body was consistently weak during the two weeks before admission. She had difficulty in naming familiar objects, and there was no other disturbance of speech.

The patient had previously been in good health. About four years before admission she went through a pregnancy without evidence of toxemia, being delivered of a normal, full-term child by cesarean section. Ten years before admission she had complained of vomiting and weight loss for about three months; there was no jaundice, but some abdominal pain.

Physical examination revealed a poorly developed

and nourished woman. The lips and skin were dry. The breasts were enlarged, tender and lactating. The left axillary lymph nodes were tender. The heart and lungs were normal. The abdomen was soft, and no masses were palpable.

The patient was euphonic, and speech was indistinct. Her voice was weak; she lost interest rapidly and had a small range of ideas and a poor memory. The pupils were equal, each measuring 5 mm. in diameter; the left was irregular and did not react to light. There were no specific weaknesses of the extraocular muscles, but eye movements were not carried so far to the left as to the right. The patient stated that she had had intermittent diplopia, worse when she was not looking straight ahead. There was papilledema of 3 diopters on the right, and 5 diopters on the left. Visual acuity was greatly diminished. The visual fields were apparently normal. A right facial paresis was present. Auditory acuity was slightly diminished on the left. The neck was slightly stiff, and a Kernig sign was present. Motor weakness was generalized, more marked on the right than on the left. The tendon reflexes were bilaterally hyperactive, particularly on the right, and there was ankle clonus bilaterally, more marked on the right than on the left. The abdominal reflexes were absent. The plantar reflex response was extensor on both sides.

The temperature was 99.2°F., the pulse 100, and the respirations 20. The blood pressure was 110 systolic, 55 diastolic.

The urine on admission contained no sugar but gave a ++ test for acetone; the sediment contained 10 white cells per high-power field. The red-cell count was 3,700,000, and the white-cell count 12,000; the hemoglobin was 11.5 gm. per 100 cc.

A lateral x-ray film of the skull showed a calcified plaque in the parietal region. On ventriculography, the fluid in the right ventricle was under increased pressure, which rapidly fell to normal. A large mass appeared to be present in the left frontal region; this markedly depressed the left anterior horn and forced the ventricles, including the third, to the right. The ventricles were not distended. Electroencephalography revealed focal disturbance, greatest in the left frontal region.

A left frontoparietal craniotomy was done on the first hospital day, and 65 cc. of thick, brown fluid was aspirated by needle. The patient's immediate postoperative condition was poor. She was unresponsive, with fixed pupils and ankle clonus. All other reflexes were absent. A lumbar puncture revealed slightly bloody spinal fluid under an initial pressure equivalent to 450 mm. of water; the final pressure was 100 mm. The blood pressure remained almost constant at 90 systolic, 60 diastolic. The pulse varied from 140 to 160, and the temperature from 100 to 105°F. Although she received 1500 cc. of whole blood and 1500 cc. of glucose in water, she remained unconscious. A second lumbar puncture also yielded bloody fluid under an initial pressure equivalent to 400 mm. of water; after slow withdrawal of 10 cc. the pressure fell to 180 mm.

Late on the first postoperative day the respirations became markedly slowed. An hour later respirations ceased, with persistence of the heart beat for a short time longer.

Differential Diagnosis

Dr. Jost Michelsen: It is not difficult to decide that this patient had a space-occupying lesion. There were characteristic manifestations of increased intracranial pressure, such as severe headache, nausea and vomiting, failing vision, drowsiness and papilledema. We are also given the localization of the lesion. It involved the left side of the brain, producing weakness of the right side of the body and probably also the disturbances of the oculomotor mechanism by damage to Area 8. The ventriculogram showed a mass in the left frontal region, the electroencephalographic studies were consistent with a lesion there, and I presume that the fluid-containing cavity was found in the same area.

Reviewing briefly some of the signs, I am not certain whether the anomia was actually found on examination or whether some of the patient's complaints were interpreted as an amnesic aphasia. We are not told, either, whether she was right or left handed. If her dominant hemisphere was on the left side, a frontal lesion should have produced a defect in word formation rather than anomia.

Another observation deserves some comment. It is said that the left pupil was irregular and did not react to light and that both pupils were fairly wide and equal. The irregularity may have been due to an old lesion of the iris. The absence of the light reaction probably was the result of severe damage to the left optic nerve; in other words, the patient was blind in the left eye. The fact that the papilledema on the left side was 5 diopters — as compared with 3 diopters on the right side — is certainly suggestive. One would be more certain with regard to this point if the findings on testing the consensual light reaction were known and recorded.

It is obvious that the most important question to be answered in this case is that concerning the character of the mass. If we attempt to make a preoperative diagnosis in the average case we take into account the age of the patient, the history, the situation of the lesion and the radiographic appearance of the skull. In this case we are also informed about some of the findings at operation. The surgeon aspirated 65 cc. of thick, brown fluid, which indicates that there was a large cyst, and we shall have to form an opinion concerning the type of this cyst.

The history contains quite a few details of the patient's pregnancy, and this case was announced on the bulletin board as one with cerebral symptoms following pregnancy. Considering all the evidence

offered, I do not hesitate to disregard the apparent toxemia during the early course of her pregnancy as an etiologic factor. I believe that the appearance of symptoms during her pregnancy — as in some other cases that we have seen — was entirely incidental and perhaps quite misleading to her family physician. Occasionally in a slowly growing tumor exacerbation of manifestations is observed during pregnancy. Dr. B. Brouwer,* of Amsterdam, observed a patient who, during her sixth pregnancy, developed a bitemporal hemianopsia. It was thought that this was a complication of her pregnancy. Indeed, after delivery her visual fields became normal. With her seventh, eighth and ninth pregnancies she also had transient bitemporal hemianopsia. After delivery of her tenth child, however, the hemianopsia persisted. She then developed headaches, and it turned out that she had a parasellar meningioma.

It is also hardly conceivable that the patient had a parasitic cyst. There was no evidence of cysts elsewhere in the body. There was no eosinophilia. The character of the aspirated fluid was different from that found in a parasitic cyst.

A bacterial infection is quite unlikely, although we are told that the neck was slightly stiff and that a Kernig sign was present. There was no adjacent or distant source of infection so far as we know.

Therefore, we must consider some of the brain tumors in which cyst formation occurs. At this point I should like to ask Dr. Schulz to say a few words about the calcification in the occipital region.

Dr. Milford D. Schulz: The calcification is in the occipital region on the right. It lies fairly close to the midline but scarcely closely enough to the midline to be outside the occipital lobe; it seems to lie above the tentorium.

Dr. Michelsen: Is it quite unlikely that the calcification has anything to do with the mass in the frontal area?

Dr. Schulz: Yes. Certainly there is a considerable distance between the two.

The anteroposterior film shows the deformation and displacement of the frontal horns. The left one is pushed down under the tentorium, and to the right, and the right one and third ventricle are displaced to the right.

Dr. Michelsen: Do you consider that the cyst represents a second lesion?

Dr. Schulz: I think that there were two separate lesions.

Dr. Michelsen: I shall rule out an astrocytoma because of the rapid course of the patient's disease, the absence of epileptic seizures and the character of the fluid. A craniopharyngioma would not have occupied the left frontal lobe, depressing the anterior horn of the lateral ventricle — these tumors arise from below in the suprasellar region. Furthermore, the clinical symptomatology in this case is against such a diagnosis.

*Brouwer, B. Personal communication.

A glioblastoma multiforme is a fair possibility. These tumors grow rapidly. The occurrence of hemorrhagic extravasations and necrosis is frequent and would account for the brown color and the consistence of the cystic fluid. We also ought to consider metastatic carcinoma, although there is little evidence in the story to support this diagnosis, except that the patient was in poor shape and had acetone in the urine as an indicator of malnutrition.

There is one other type of tumor, however, in which thick, brown fluid is fairly characteristic. Was a microscopic examination done on the fluid?

Dr. Charles S. Kubik: That was done, and there were large vacuolated cells that probably contained fat. Such cells are present in the cystic fluid of various kinds of tumors. There were no cholesterin crystals.

Dr. Michelsen: Dr. Kubik has anticipated my thought. I had in mind a dermoid cyst. These tumors are rare. They are usually located in the midline, basally, but they may occur in the different lobes of the forebrain. At times they are multiple. They grow at a very slow rate and may attain a considerable size before resulting in symptoms.

Now let us search for the cause of death. This patient was a nearly hopeless surgical problem from the onset. Her general condition and nutrition were poor, as mentioned before. She had bilateral pyramidal-tract disturbances, which I have omitted from the discussion so far. They, and possibly also the rigidity of the neck and the Kernig sign, seem to indicate that there was some tentorial herniation preoperatively as a result of markedly increased intracranial pressure. This condition apparently was not relieved by the removal of the cyst fluid; indeed it progressed, and the two postoperative lumbar punctures certainly did not help the situation. The patient developed hyperthermia and respiratory failure.

In conclusion, I should say that this patient had a brain tumor and that during the last few days of life a tentorial pressure cone occurred, which resulted in death. The tumor may have been a malignant, necrotic, hemorrhagic glioma, a dermoid cyst or possibly a metastatic carcinoma. I am prepared to hear that it was none of the three.

Dr. Benjamin Castleman: Would you like to say a word about this patient's pregnancy, Dr. Newell?

Dr. John L. Newell: I do not see how the tumor could have been associated in any way with the pregnancy, which was a full-term cesarean delivery. The vomiting and headache were probably passed off as being due to the pregnancy, and this was undoubtedly misleading.

Clinical Diagnoses

Brain tumor.
Respiratory failure.

Dr. Michelsen's Diagnoses

Brain tumor (glioma, dermoid cyst or metastatic carcinoma).
Tentorial pressure cone.

Anatomical Diagnoses

Adenocarcinoma of lung, with metastases to bronchial lymph nodes and brain.
Tentorial pressure cone, with cerebral infarction.

Pathological Discussion

Dr. Castleman: Before I tell you what was found at autopsy perhaps Dr. Kubik would like to tell what was found in the brain grossly.

Dr. Kubik: In the left frontal region there was a tumor a large part of which was taken up by a cystic cavity measuring 2.5 cm. in diameter and containing a small amount of coagulated brownish fluid. The cavity was naturally much larger before the cyst was drained at operation. There was an exceedingly large temporal pressure cone on the left side, and a smaller one on the right, with resulting compression of the midbrain. The aqueduct was flattened to the point of obstruction. There was a small hemorrhage in the midbrain in the region of the third-nerve nuclei. Either the compression of the midbrain or the implication of the third nerves might have accounted for the diplopia and the dilated fixed pupils. There was also extensive, recent, hemorrhagic necrosis of a large part of the left cerebral hemisphere. Such necrosis, resembling hemorrhagic infarction, is not infrequently observed with a temporal pressure cone, but the infarcted region is usually the one supplied by the posterior cerebral artery, presumably because this artery is compressed by the inner edge of the tentorium. I do not know how to account for infarction in this case, because the infarcted regions are supplied by both the posterior and middle cerebral arteries. There was also a large cerebral pressure cone, which no doubt accounted for the respiratory paralysis. It is reasonable to suppose that both the temporal and the cerebellar pressure cones were made worse by the lumbar punctures.

Dr. Castleman: The tumor microscopically was a metastatic carcinoma. The primary source was in the right upper lobe bronchus. Unfortunately an x-ray film of the chest was not taken. There was an ulcerating tumor in the bronchus, with extension to the surrounding parenchyma of the lung and with metastases to the bronchial lymph nodes.

The uterus was enlarged. It had not completely involuted, and in the endometrium were shaggy clots, which allowed us to toy with the idea, based on the gross findings, that it was a chorionepithelioma with metastases to the lung and brain. Histologically, however, the tumor was an extremely rapidly growing adenocarcinoma and not a chorionepithelioma.

The pregnancy may well have made the tumor grow much faster, and this rapid growth of the tumor cells may have accounted for the fact that the tumor was cystic, that is, it had broken down because it had outgrown its blood supply. The bronchial lymph nodes were also necrotic.

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PHYSICAL FITNESS AFTER THE WAR

The ineligibility for military service of over 30 per cent of the men examined under Selective Service is one of the outstanding health facts uncovered by the war, and those who have used the war as a sounding board for their prewar convictions are already exploiting this fact by resolving in public, as usual, that such a thing must never happen again. To say, on the other hand, that physical standards for large bodies of men were never before so high as they are in our armed forces is merely to state the obvious. So far as the medical profession is concerned, it has a definite obligation to give this matter its attention, to formulate its opinion and to raise its voice in the current political discussion.

How can we reduce to a minimum the physical defects of another generation? There are, to begin with, certain obstacles of an emotional nature with which we shall continue to contend, and we must also recognize the biologic fact that no seed is of uniformly high quality. Nurserymen and raisers of livestock know that nature with its infinite variety, produces, even with the best seed and stock, a considerable percentage of imperfectly formed specimens — stunted plants or runts. The nurseryman and farmer cull these from their crop or herd, being under no compulsion to raise them, although, of course, they could, with time and patience, nurse many of them to maturity. We have no such freedom of action in human nurseries: ours is a civilization in which we strive for the protection and survival of the unfit.

The medical profession's major activities have for years been concerned with such protection and survival, and in view of its accomplishments and its support by the public it is today actually responsible for the survival of many of those who have been found ineligible for military service; in other words, we have reversed the philosophy and the practice of the ancient Spartans. We must also recognize that, in many places, legal and political impediments have been placed in the way of parents who may have biologic as well as economic reasons for controlling the birth of their offspring. These are the obstacles — paradoxic and perhaps insurmountable — with which our civilization contends and will contend at the close of the war. In view of them the conditions revealed by the statistics of the Selective Service and induction boards are not at all amazing; they are only what might have been expected, although many of us have been startled by the fact in this period of national crisis.

The greatest difficulty with which we are confronted in attempting to reduce the numbers of the physically unfit in a democracy is the freedom of the individual to neglect himself. It would be a good freedom to abolish if such a thing were justifiable, and the medical profession should support any reasonable steps likely to promote physical fitness.

At the present time there are two political rings into which the profession can throw its hat. The first is the constructive health-education program

that has been adopted by many cities and towns outside Boston, largely owing to the efforts of the Massachusetts Department of Public Health and Department of Education, and that is recommended by the Strayer Report as a procedure that might well be adopted in the schools of Boston. This is something that doctors can approach locally, where they can tactfully secure what intimate knowledge of existing conditions is necessary to initiate a reform, good medical leadership of this type being seldom challenged. The other political ring is that which encircles those who are now debating peacetime military training. Here will be found a sharp cleavage of opinion — one in which the clergyman, the professional soldier, the statesman, the businessman, the educator and many other intelligent people are divided among themselves. This being so, and in view of the biologic and psychologic facts that every doctor knows, it is the duty of organized medicine and of each individual physician to throw themselves vigorously into the debate in favor of peacetime conscription.

Even in wartime the Army has rehabilitated close to two million men; in peacetime it could unequivocally eliminate many of the correctible defects that are now neglected by parents, school authorities and individuals. Universal military training in peacetime would do more to improve the physical fitness of the Nation's young men than any other method that could be devised. There should be no division of opinion in the medical profession on this issue.

SPREAD OF STREPTOCOCCAL INFECTIONS

During World War I, hemolytic streptococcus infections were the most serious and the most frequent complications of measles and influenza, as well as of wounds, and they probably accounted for a great many of the deaths ascribed to these conditions in the United States Army. The rapid spread of such infections in Army hospital wards was the subject of numerous studies at that time. The recognition of specific groups and types of hemolytic streptococci during the last decade has given epidemiologists a highly useful tool whereby they can trace the sources and spread of such infections with reasonable assurance and accuracy. Although hemolytic streptococcus infections are not nearly so prevalent now, either in civilian or in military populations, as they were during the first world war, they still constitute an important problem at certain Army and Navy installations. Hence, various groups of workers have been engaged in studying these infections. Among them, the Commission on Air-Borne Infections has obtained useful information concerning the quantitative aspects of the transmission of hemolytic streptococci in Army hospital wards.

Hamburger,[1] in a report of some of these studies, re-emphasized certain of the known facts and brought out some new and useful ones that are essential for the control of infections with these organisms. He found, for example, that gross infections by hemolytic streptococci on open wards may spread rapidly when only as few as one or two carriers are originally present. On the other hand, as many as 50 per cent of the patients on a ward may harbor Group A streptococci in their throats without cross infection's occurring in any of the others. On the average, the carrier rate for a specific type known during the same season to be invasive may be as high as 19 per cent without the occurrence of cross infection. "Subclinical cross infection," that is, a spread of carriers or of cases of mild infection by hemolytic streptococci, was quite frequent.

As already indicated, outbreaks of measles have been known to encourage the spread of hemolytic streptococci and to give rise to serious respiratory complications with these organisms. During the present war, cases of German measles have been unusually prevalent. This disease is ordinarily considered to be a mild one of little or no consequence. In the present investigations, however, Hamburger found that patients recovering from German measles share the well recognized susceptibility of those with measles to streptococcal infections.

In the course of tracing the origin of cross infections with streptococci, emphasis was placed on the importance of typing the streptococci before a member of the hospital personnel who is a carrier can be incriminated as the source of the infection. Actual typing under such conditions may indicate that an entirely different strain is responsible for

the cross infection than the one or ones found in the carriers among the personnel. This may also be of importance in surgical practice, where the spread of streptococcal wound infections is often ascribed to a surgeon or an operating room nurse who happens to be a carrier. Such persons are often kept from the operating rooms when they are not the ones responsible for the cross infections.

Attempts were also made to determine to what extent streptococcus carriers may disseminate their strains.[2] This was done by comparing the results of throat cultures with quantitative estimations of the numbers of organisms in the saliva, the latter being presumed to be the origin of droplets from which the organisms get into the air and dust. It was found that a person with a positive throat culture may or may not have the same organism in the saliva. In cases of active sore throat, to be sure, over 80 per cent of the specimens of saliva contained the same strains of streptococci as were found in the throat cultures, but the rest had no streptococci in the saliva. The relation of the positive throat and salivary cultures in any patient varied from day to day. In about half the cases the number of hemolytic streptococci in the saliva diminished in successive samples, usually gradually but sometimes quite abruptly. In about a fourth of the cases the results of repeated cultures were the same over a period of weeks, about half of these having positive and the other half negative cultures of the saliva. Cases of scarlet fever and those of pharyngitis or tonsillitis without a rash behaved alike with respect to the number of streptococci in the saliva. Tonsillectomized patients tended to carry fewer streptococci in the saliva, and for shorter periods, as compared with those who had tonsils. None of these findings had any relation to the type of the streptococci. Interestingly enough, treatment with sulfonamides did not permanently eliminate or decrease the numbers of hemolytic streptococci either in the throat or in the saliva.

Since the commission was interested primarily in air-borne infections they made extensive studies of hemolytic streptococci in the air, floor dust and bedclothes in the hospital wards.[3] The great difficulty of proving that cross infections in a ward are truly air borne, and not spread by contact, was emphasized. One case was noted of a technician in whom there was a strong suspicion of accidental air-borne infection from prolonged exposure at a distance from patients. This technician was engaged in taking air samples, and it was calculated that the total dose that she inspired was about 13,000 organisms.

Many known epidemiologic facts about hemolytic streptococcus infection in the environment were confirmed by accurate methods. It was found, for example, that the rise and fall in the number of streptococci in scarlet-fever and sore-throat wards paralleled the fluctuations in the total numbers of bacteria in the air, although the streptococci constituted a small part of the total. Most of the other organisms were saprophytes and, therefore, probably arose from dust and bedclothes, which contain tremendous numbers of bacteria. Pockets of high concentrations of hemolytic streptococci were associated with high concentrations of saprophytes during periods of sweeping or bedmaking. The largest numbers of streptococci were found in the air dust and in the bedclothes nearest those patients who actually eliminated the largest number of streptococci.

On the basis of their observations, the members of the commission were not able to determine accurately the exact role of air-borne and dust-borne infections. They suggested, however, that the control of air-borne streptococci in hospital wards may be largely a question of controlling the secondary reservoirs of these organisms in the dust and bed linens. The results of studies in which this was attempted seem to indicate that such control is feasible. The maximum reductions in air-borne streptococci were observed when oiling of the bedclothes and floors was used in conjunction with glycol vapor.[4]

References

1. Hamburger, M., Jr. Studies on transmission of hemolytic streptococcus infections. I. Cross infections in army hospital wards. *J. Infect. Dis.* **75**:58-70, 1944.
2. *Idem.* Studies on transmission of hemolytic streptococcus infections. II. Beta hemolytic streptococci in saliva of persons with positive throat cultures. *J. Infect. Dis.* **75**:71-78, 1944.
3. Hamburger, M., Jr., Puck, T. T., Hamburger, V. G., and Johnson, M. A. Studies on transmission of hemolytic streptococcus infections. III. Hemolytic streptococci in air, floor dust, and bedclothing of hospital wards and their relation to cross infection. *J. Infect. Dis.* **75**:79-94, 1944.
4. Robertson, O. H., et al. Study of nature and control of air-borne infection in army camps. *J. A. M. A.* **126**:993-1000, 1944.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

TALTY — Francis E. Talty, M.D., of Hoboken, New Jersey, died on May 27. He was in his sixty-sixth year.

Dr. Talty received his degree from Harvard Medical School in 1906. He was a member of the New England Roentgen Ray Society.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE, 1945

RÉSUMÉ

Diseases	June 1945	June 1944	Seven-Year Median
Anterior poliomyelitis	2	1	1
Chancroid	1	4	*
Chicken pox	1282	1748	1170
Diphtheria	14	6	7
Dog bite	1299	1186	1414
Dysentery, bacillary	1	2	2
German measles	139	199	199
Gonorrhea	378	442	355
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	1	4	*
Malaria	92	59	1
Measles	1409	3011	3918
Meningitis, meningococcal	19	28	16
Meningitis, Pfeiffer-bacillus	2	0	4†
Meningitis, pneumococcal	3	3	3†
Meningitis, staphylococcal	0	0	0†
Meningitis, streptococcal	2	0	0†
Meningitis, other forms	2	1	2†
Meningitis, undetermined	3	7	4†
Mumps	1677	966	877
Pneumonia, lobar	140	215	225
Salmonella infections	18	13	6
Scarlet fever	949	899	791
Syphilis	335	458	417
Tuberculosis, pulmonary	213	287	287
Tuberculosis, other forms	15	21	24
Typhoid fever	2	2	7
Undulant fever	6	5	4
Whooping cough	560	248	551

*Made reportable December, 1943.

†Four-year average.

COMMENT

Only two cases of anterior poliomyelitis were recorded in June. It should be pointed out, however, that no conclusions can be drawn from this fact with reference to the likelihood of an outbreak later in the season. Even the July figures are not always an accurate indication of what to expect.

Lobar pneumonia showed a very low incidence — the lowest for June since 1922.

Mumps was at the lowest point of this year but was, nevertheless, at the highest level of any June on record.

Diphtheria was still higher than in recent years. Only once since 1937 has June shown as many as 14 cases.

Only once before have more than 18 cases of Salmonella infections been reported in June.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Haverhill, 1; Holyoke, 1; total, 2.

Diphtheria was reported from: Boston, 3; New Bedford, 2; Newton, 1; Norwood, 1; Somerville, 5; Taunton, 1; Worcester, 1; total, 14.

Dysentery, amebic, was reported from: Regional Hospital, Waltham, 1; Camp Edwards, 2; total, 3.

Dysentery, bacillary, was reported from: Wrentham, 1; total, 1.

Malaria was reported from: Arlington, 1; Boston, 3; Camp Edwards, 17; Fort Devens, 55; Gloucester, 1; Lawrence, 1; Norwood, 1; Somerville, 1; Springfield, 1; Waltham Regional Hospital, 11; total, 92.

Meningitis, meningococcal, was reported from: Attleboro, 1; Boston, 6; Dedham, 1; Fall River, 1; Holyoke, 2; Ipswich, 1; Lynn, 1; Malden, 1; Newton, 1; Norwood, 1; Quincy, 1; Randolph, 1; Topsfield, 1; total, 19.

Meningitis, Pfeiffer-bacillus, was reported from: Arlington, 1; Cambridge, 1; total, 2.

Meningitis, pneumococcal, was reported from: Boston, 3; total, 3.

Meningitis, streptococcal, was reported from: Boston, 1; Worcester, 1; total, 2.

Meningitis, other forms, was reported from: Boston, 2; total, 2.

Meningitis, undetermined, was reported from: Brookline, 1; Springfield, 2; total, 3.

Salmonella infections were reported from: Boston, 3; Cambridge, 1; Haverhill, 1; Malden, 1; Marblehead, 6; Newton, 2; Northampton, 1; Salem, 2; Wellesley, 1; total, 18.

Septic sore throat was reported from: Boston, 4; Easton, 4; Haverhill, 1; Lynn, 6; Medford, 1; Sharon, 1; Williamstown, 3; total, 20.

Typhoid fever was reported from: Lowell, 1; New Bedford, 1; total, 2.

Undulant fever was reported from: Adams, 1; Dighton, 1; Sheffield, 1; Waltham, 1; West Boylston, 1; Williamstown, 1; total, 6.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Clinic Consultant
Lowell	August 3	Albert H. Brewster
Springfield	August 21	Garry deN. Hough, Jr.
Fall River	August 27	Eugene A. McCarthy

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Textbook on Pathology of Labor, the Puerperium and the Newborn. By Charles O. McCormick, M.D., clinical professor of obstetrics, Indiana University School of Medicine, and consulting obstetrician, William H. Coleman Hospital for Women, Indianapolis City Hospital and Sunny Side Sanitarium. 8°, cloth, 399 pp., with 191 illustrations, including 10 in color. St. Louis: The C. V. Mosby Company, 1944. $7.50.

The author's lectures, prepared for the senior medical students at Indiana University, have served as a basis for this new work on the pathology of labor. An attempt has been made to set forth only the essentials of present-day obstetrics, purposely avoiding confusing textbook material. Special consideration has been given pelvimetry, breech extraction, placenta previa, post-partum hemorrhage, use of forceps, version and cesarean-section technics, puerperal infection, breast pathology and asphyxia neonatorum. There are detailed descriptions of therapeutic and surgical procedures, of tubal sterilization operations and of the newer therapeutic adjuncts, such as puerperal sterilization, sulfonamides, penicillin and stilbestrol, vitamin K, erythroblastosis and improved analgesia. The book is well illustrated and printed on good paper. References to medical literature have been incorporated in the text instead of placing them at the end of chapters.

Technique of the Standard Kahn Test and of Special Kahn Procedures. By Reuben L. Kahn, chief of clinical laboratories, University of Michigan Hospital. Revised and enlarged edition. 8°, paper, 52 pp., with 4 tables. Ann Arbor: University of Michigan, 1944. 25 cents.

In this revised and enlarged outline, Dr. Kahn presents the technic of the standard Kahn test with serum and spinal fluids, the interpretation of precipitation results and technics of special procedures, with an appendix on the preparation and standardization of antigen. The pamphlet is divided into four parts, with an appendix: apparatus; reagents; standard Kahn procedures; and special Kahn procedures.

(*Notices on page xvii*)